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THE AMERICAN
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VOL. 105 SEPTEMBER, 1933 No. 9

EDITORIAL

THE NEW DEAL FOR FOOD AND DRUG CONTROL

IN 1906, during a Roosevelt administration, the Pure Food and Drugs Act was passed. Its subsequent enforcement revolutionized food and drug manufacture and made these commodities far saner and safer than ever they had been before.

Indeed, in the so-called "good old days" prior to its passage, incredible things had been done—unbelievable licenses and liberties had been taken with materials intended for feeding and medicating our people. Mis-labeling, adulteration, label-lying, substitution, stretching (increasing the inert), and many other such odious practices were commonplace and flagrant.

Babies were swindled to sleep with soothing syrups, poppy-doped and pleasant—veritable morphine lullabies; children's candies, covered with shellac, carried many a gastric shock, lampblack for licorice, talcum for starch and saccharin for sugar.

Milk men plied the pump and kept their product five-day sweet with corpse-preserving fluid (formaldehyde).

Chromate of lead, an intensely yellow pigment and poison to boot, was once a food ingredient. Philadelphia bakers, knowing no better, used this vicious compound, to give their cakes the egg color and complex. Think of it—angel cake—colored with chrome yellow. And how mathematically accurate!—One cake—one angel!

And so we could continue on and on with our story of the "good old days" before the Food and Drugs Act really went to work.

But things were changed from that eventful day in 1906—and food and drugs were manifestly safer.

The Department charged with the operation of this Federal law, and State Departments functioning in a like capacity, maintained a jurisdiction over edibles and medicines, such as had never been maintained before.

Yet, as time progressed and practices changed, the Act of 1906, as might be well expected, became quite inadequate. It was too limiting in its provisions, and minor amendments to it only made for temporary results. The need for greater scope and authority for the act and its agents is seen in the continued infractions of the present law.

For instance, the United States Department of Agriculture, in recent judgments under the Food and Drugs Act, includes the following articles of delicatessen(?): excessive mold in canned blackberries; decomposed sardines, tuna fish and salmon; excessive mold in tomato catsup; decomposed canned sweet potatoes; butter below standard weight of milk fat and below weight designated on package; decomposed canned shrimp; celery containing arsenic in amount which might have rendered the article injurious to health; decomposed canned prunes; cheese deficient in fat and containing excessive moisture; canned tomatoes containing an excessive amount of blemished and excessive peel; dried cherries which were insect-infested, moldy and dirty; dressed poultry which was in part diseased and decomposed; arsenic and lead in dangerous quantities in raw apples; dried grapes which were decomposed and insect-infested; cabbage containing excessive amounts of arsenic; olive oil samples containing little or no olive oil, and of domestic manufacture when the label indicated that it was a foreign product; walnut meats which were in part decomposed, moldy and wormy; fresh blueberries found to contain maggots.—All of which is food unfit even for thought.

And now from foods to face-pads. Once, in the not so very long ago, the cosmetic urge was a puny little impulse. Now, however, it is grown to a comic splurge, and none there is to regulate it.

Once, too, the advertising business was not so brazen and bold. Today there is no end to its effrontery.

Nor was there in the 1906 Act any legal way to control these features of food and drug disposal. Of course, the label on the package had to tell the truth, more or less, yet advertising copy—whether massed on the printed page or messed through the medium of the ether—was totally beyond the sway of the Act.

Then, too, there are always those unscrupulous producers ever in search of loopholes and ever alert to the chance for a technical evasion of law. And the original law did invite evaders.

All of these things and more, contributed to the inadequacy of the 1906 Act. Through several administrations efforts had been

made to improve it or to substitute for it, legislation more forceful and up to date.

It is strikingly coincidental that another Roosevelt administration should now be responsible for what we shall soon have as the New Pure Food and Drug Act.

Its passage will be part of the New Deal—and a great deal can be expected of it.

From the *Industrial Bulletin* of the Arthur D. Little organization in Massachusetts, we cull this well-written survey of the Act, quoting it in full, so well and so thoroughly is it written.

"Let the seller beware" is slated to become fully as much a warning to the food, drug, and cosmetics trades as the recent Federal Securities Act has made it a warning to the investment banker. For the "new deal" includes a bill which so thoroughly revises, strengthens, and extends the Pure Food and Drug Act of 1906 that, like the securities bill, it will both necessitate drastic changes in the practise of less scrupulous companies in these trades and occasion considerable care on the part of more reliable companies, whom it should ultimately benefit. This bill (S. 1944), apparently drawn as part of the Administration program, has won a large measure of support among manufacturers heretofore generally opposed to such legislation. Although certain to be modified to some degree, it is expected to be passed this winter without substantial change.

Drastic innovations in the regulation of advertising are among the most significant provisions of the proposed bill. Advertising of any sort—printed, radio, or by salesman—will be subject to the same official scrutiny now given the label on the package. Direct misstatement, ambiguity, obvious omissions, and misleading natural inferences,—all will constitute falsification. Claims are to be judged on the quality of the product rather than on freedom from intent to deceive. Imitations must be plainly so labeled.

Food adulterations, the proposed bill provides, are to be considered from two viewpoints: Hygienic adulteration, which has to do with anything prejudicial to the health of the user, and economic adulteration (stretching) as by slack filling of packages, dishonest bottles, or short weight, which affect his pocketbook. Hygienic considerations start with the raw materials and methods of manufacture, and extend to the influence of the containers on the product.

Drugs would include, not only medicinals, but also such items as surgical dressings, therapeutic devices, depilatories, and obesity cures. The U. S. P. and N. F. specifications of strength and purity are slated to be minimum standards under the act, but the Government is to be further authorized to set its own standards. Drugs come under the ban of the code if they may have an adverse cumulative effect under ordinary use, or if, even though they remedy the ailment, they are

dangerous to general health when used as prescribed. No product will be allowed for sale to the public for purposes where self-medication is futile or dangerous. All hypnotic or narcotic substances, and all active ingredients present which are not prescribed in the U. S. P. or N. F., must be declared on the label. Antiseptics must be specified as to killing time and concentration for the organisms to be killed.

"Cosmetics," which are to include "all substances and preparations intended for cleansing, or altering the appearance of, or promoting the attractiveness of the person," are to be under as strict limitations in advertising and labeling when the bill is enacted as are foods and drugs. They must contain no poisons in violation of regulations, and must not be dangerous to the user, under the conditions of use, in any way. Since cosmetics are, however, to be judged as finished products rather than for the individual materials they may contain, considerable opportunity will remain for the exercise of ingenuity in devising new types and compositions.

The administrative powers of the Secretary of Agriculture would be greatly broadened under the new bill. They would include the right of executive seizure of whatever he judges improper under the act (with the burden of proof of propriety falling upon the manufacturer), authority to require permits in those cases where the products are dangerous to health or where possible injurious action cannot be ascertained by objective inspection, and the right to inspect manufacturing plants. His proposed authority to permit the use of safe coal-tar colors and presumably preservatives, etc., and to establish reasonable tolerances for poisons, should afford more reasonable regulation for manufacturers.

That enactment of the bill will necessitate sweeping changes in the products and practices of many manufacturers is obvious. Some products must be radically changed in order to avoid proscription under it; many more must be greatly improved if they are to come anywhere near to satisfying their advertising claims, to which they will be strictly held. In many cases care must be taken that such improvements may be made without changing the characteristic appearance of the product. Since the scant six months to intervene between the passage of the act and the date it takes effect may in many instances be altogether inadequate for the amount of work required to meet the provisions of the act, a number of manufacturers have already begun work upon their products. It seems altogether probable that one effect of the bill will be the development of products superior to any now existing, through work undertaken to prepare products for the new requirements.

We must bear in mind, however, that the foregoing is *proposed* legislation, and there is no telling how the provisions of the act may be finally emasculated by inspired and perspired legislators.

IVOR GRIFFITH.

ORIGINAL ARTICLES

A STUDY OF THE PROPERTIES OF PSYLLIUM SEED

By Rachel Hansche and E. U. Still

From Pacini Laboratories, Inc., 155 East Ohio St., Chicago, Illinois

THE seed of the Plantago Psyllium plant, commonly called Psyllium Seed, has been recommended as a mild laxative agent.

Although Psyllium Seed has been used for various therapeutic purposes in Europe and Asia, it is only within the last few years that it has been introduced into the United States and, judging from the quantities imported, it has met with considerable popularity.

Psyllium Seed is listed in the United States Dispensatory [1] as a mild laxative to be used in cases of chronic constipation. Solis-Cohen and Githens [2] describe its usefulness as a therapeutic agent in constipation and other conditions. Fantus [3] says, "Its action might be considered as a combination of bran and agar."

Montague [4] in his book states on page 127, "Psyllium seeds seem to meet the requirements for a non-irritating, bulky lubricating substance better than either of the foregoing. The seeds, except for the exuded lubricating jelly, remain intact. They do not appear to irritate the colonic mucosa. Possibly this is due to the fact that they are relatively soft and even when finally excreted are enveloped in the demulcent jelly exuded through the pores in their testa. The psyllium exudate is in itself non-irritating and adds both bulk and smoothness to the fecal mass. Contrary to some workers with this seed, we find as described in experiments mentioned elsewhere, that this jelly is slowly digested. Owing, however, to its viscosity it does not envelope food particles as does mineral oil and it thus intrudes but to a negligible extent on the digestive processes. Finally, the seeds are practically tasteless and thus are preferred by persons who have an aversion to oily medicaments."

In view of the numerous papers which advocate the use of psyllium as a laxative, it seemed desirable to know more about the chemical composition of the seed and its parts than was given by Hepburn and Laughlin.[5]

It is the purpose of this paper to present the chemical anaylsis of the seed and its parts.

Experimental

Whole clean blond Psyllium seeds were procured and ground to pass through a 60-mesh screen. The powder was dried over Calcium Chloride and aliquots were taken for analyses.

The seeds are covered by a thin crisp hull which can easily be removed and separated. The hulls were prepared for analyses as were the whole seeds.

An aqueous extract of the hulls which contained all of mucilage and water soluble constituents was dried in vacuo and prepared for analyses as given above.

Methods of Analyses

1. Ash—Samples were ashed at a dull red temperature in porcelain crucibles until a constant weight was obtained.

2. Total Nitrogen—Appropriate samples were wet ashed and N determined by the messlerization method of Koch & McMeekin.[6] Appropriate deductions were made for blank determinations. The nitrogen values may be converted into protein content by the factor 6.25.

3. Total Phosphorus—Appropriate samples were ashed with concentrated H_2SO_4 and HNO_3. The Fisk & Subbarow [7] method was applied to the diluted solution.

4. Carbohydrate—Total carbohydrate was determined on aliquots of samples hydrolyzed for six hours at 90 degrees C. with two per cent. HCl. The same hydrolysates were used for the estimations of pentose. The pentoses were converted into furfurol by steam distillation from 12 per cent. HCl. The furfurol was converted into the phloroglucinide, filtered, dried and weighed.

5. The results reported in this paper represent data at least from duplicate analyses.

Table I gives the analytical results obtained in this study. The calculations were made on the basis of dry weight. These data were obtained from two separate series of analyses.

Our analyses upon the whole seed are in agreement with the reported work of Hepburn and Laughlin.[5] The analyses of the hulls and the extract indicate the distribution of various elements in the seed. The minerals seem to be rather uniformly distributed throughout the whole seed. Practically none of the Protein and Lipoid is

found in the hull. The hulls are composed almost entirely of a gum which is mainly of the pentosan character.

TABLE I

Substance	Moisture %	Ash %	Total N %	Total P %	Lipoid %	Total CHO as Hexose mgm %	Pentose %
Whole	7.00	2.99	2.34	0.440	9.31	117.0	12.85
Seed	8.00	3.00	2.26	0.436	7.42	109.0	11.75
Av.	7.50	3.00	2.30	0.438	8.36	113.0	12.30
Hulls	—	2.44	0.44	0.103	—	644	38.46
	—	2.62	0.44	0.101	—	639	38.62
Av.	—	2.53	0.44	0.102	—	641	38.60
Gum	—	2.54	0.12	.143	—	803	70.30
	—	2.52	0.13		—	814	86.80
Av.	—	2.53	0.125	.143	—	809	83.05

The gum is readily soluble in hot water and sets to form a fairly firm jell. By filtering a hot aqueous extract of the hulls through cotton a clear, almost colorless, preparation may be obtained. The extract may be evaporated and dried. The jell has neither odor nor flavor.

Summary

(1) Analyses have been made on whole blond Psyllium Seeds.

(2) Analyses have been made on the hulls of blond Psyllium Seeds.

(3) Analyses have been made on the gum prepared from the hulls of blond Psyllium Seeds.

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THE MICROSCOPIC IDENTIFICATION OF HEROINE

By G. D. Williams and C. C. Fulton

U. S. Industrial Alcohol Laboratory, Minneapolis, Minn.

THERE are a number of fine color tests for heroine which make its identification fairly easy. These color tests, however, with Froehde's, Mecke's, Marquis', and similar reagents, are identical with the reactions of morphine. Something more, therefore, is needed. There is, to be sure, the nitric-acid reaction of heroine, yellow changing to bright green. This is highly characteristic, perhaps specific, though not so very sensitive, and sometimes uncertain. Even if the nitric-acid test is obtained, one likes to have a direct positive test for heroine of another type. Several good microscopical tests are available.

When classified by alkaloidal precipitation, heroine belongs to the same class as cocaine. Cocaine has somewhat the greater absolute sensitivity to phosphomolybdic acid and is also slightly more sensitive, relatively, to some of the other reagents, but most of the relative sensitivities are the same.

The following table shows the relation of heroine to most of the important alkaloidal reagents, including all that give good crystals with heroine, so far as our observations have shown. The numerals state the sensitivity of the reagents in "phosphomolybdic-acid units." For example, Platinum bromide (4) requires four times as great a concentration of heroine to give a just-visible precipitate as is required by phosphomolybdic acid. Solutions of different strengths were made by repeatedly doubling the volume, starting with the strongest solution, which was 4 per cent. or 64 units. Tests were made on solutions of heroine hydrochloride, the usual salt, and also on solutions of free heroine dissolved in dilute acetic acid. The latter gives the more accurate values for sensitivity, but the differences are slight. The reagents giving any crystals are underlined.

Crystals with Mayer's & KI, Mercuric Na Bromide, and $HgBr_2$ were noticed only with the hydrochloride of the alkaloid, not with the acetate. Bromomercuric acid with the acetate crystallizes only a very little or only very slowly.

Marme's reagent and cadmium iodide give crystals, needles in rosettes, but they are either very few or form very slowly. Stannous hydrobromic acid crystallizes partially in rosettes.

HEROINE (acetate)
(or hydrochloride)

solution 1 equiv. to 1:1600 strongest solution 64, or 4%

Phosmolibdic acid—1
Silicotungstic acid—1
Br in NaBr—⅛
Bromine water—⅛
Wagner's No. 1—1/16
Wagner's No. 4—⅛
Wagner's No. 6—½
Wagner's No. 8—1
Dragendorff's—⅛
Stannous hydriodic acid —1
Mayer's—¼
Mayer's & KI—1
Marme's—1
HgI_2-NaBr—¼
HgI_2-HBr—½
HgI_2 in excess NaBr—1
Platinum Na Thiocyanate—½
Mercuric K Thiocyan. —1
Gold bromide—¼
Gold bromide & HCl—½
Mercuric Na Bromide—½
Bromomercuric acid—½
Gold chloride—½
Tannic acid & NaAc—1

Nessler's—4
HgI_2-NaCl—2
HgI_2-HCl—8
Silver Na Iodide—2
Reinecke's salt—2
Cobalt Na Thiocyan.—16
$HgBr_2$ in excess NaBr —4
$HgBr_2$ in HCl—8
Stannous hydrobromic acid—8
Platinum bromide—4
Platinum Br & HCl—8
Gold chloride & HCl—2
Gold Cl in concd. HCl —4
Mercuric Na Chloride —8
Chloromercuric acid—8
$HgCl_2$ & excess NaCl —16
$HgCl_2$ & HCl—16
Platinum chloride—8
Platinum Cl & HCl—16
Palladium chloride—16
$BiCl_3$ in HCl—16
Picric acid—2 to 1
Na Picrate—2
Trinitroresorcin—2
Alizarin Na Sulfonate —8
NH_4Molybdate—4
Na Phosphomolybdate—2
Concd. CrO_3—16
CrO_3 & HCl—8
Gold Cyanide—16
Platinum cyanide—8
Mercuric Na Chloro-Nitrite—16

Zinc K Iodide—32
Concd. KI—64
Nickel Na Thiocyanate 32
Concd. NaSCN—64
$HgBr_2$—32
$SnCl_4$ in HCl—32
$FeCl_3$ in HCl—32
$SnCl_2$ in HCl—32
$HgCl_2$—32
Tannic acid—32
Saccharin—no ppt.
$K_2Cr_2O_7$—32
Perchloric acid—32
NaOH—32, dissolving
NH_4OH—32
Na_2CO_3—32
Borax—32
Na_3PO_4—32
KCN—32
K_2CrO_4—no ppt.
Na_2HPO_4—no ppt.
Concd. KAc—no ppt.
Na Nitroprusside—64
K ferricyanide—64
K ferrocyanide—no ppt.
Mercuric Na Nitrite —no ppt.

Heroine gives good crystallization with seven different kinds of reagents:

I. Dragendorff's reagent, bismuth potassium iodide.

II. Mercuric iodide reagents, particularly HgI_2 in NaBr, HBr, NaCl, or HCl solution.

III. Gold bromide and gold chloride reagents.

IV. Mercuric chloride reagents.

V. Platinum chloride reagents.

VI. Organic reagents: picric acid, sodium picrate, and sodium alizarin sulfonate.

VII. Basic reagents: Na_2CO_3, NH_4OH, KCN, borax, and Na_3PO_4.

Stephenson in "Some Microchemical Tests for Alkaloids" (Lippincott, 1921) has described and pictured crystals with $HgCl_2$ (used with the hydrochloride of the alkaloid), picric acid, and KCN, and has also described the crystals with Na_2CO_3 and with platinum chloride (types IV, V, VI, and VII).

The Crystals

I. Bismuth Iodide Crystals.

Dragendorff's Reagent Double Strength gives good crystallization although gradual. The crystals are small roundish orange grains or equally small dense rosettes of needles or plates. Because of the smali size of the crystals this is not one of the best tests.

II. Mercuric Iodide Crystals.

A saturated solution of HgI_2 in 10% HCl gave the most rapid crystallization of reagents tested. In the more concentrated solutions, 64 to 16, the crystals are mainly branching threads; in the more dilute solutions they are plates or slender crystals, needles to blades. Crystals form down to solution ½ (1:3200) on standing. A saturated solution of HgI_2 in a 30% NaCl solution gives similar crystals more gradually.

Saturated solutions of HgI_2 in 5% NaBr, HgI_2 in 5% by volume concentrated HBr, and also 2 gm. HgI_2 with 25 gm. NaBr in 100 cc. water, give good crystallization, mainly branching crystals in solution 2 and more concentrated solutions, small needle-like crystals in very dilute solution.

Mayer's reagent, a saturated solution of HgI_2 in KI, gives very slow and generally incomplete crystallization. In dilute solution the crystals are needle-like, broadening into a small plate at one end; in more concentrated solutions they form sheaves.

III. Gold Bromide and Gold Chloride Crystals.

Gold bromide (brom-auric acid) gives gradual crystallization, mainly in brownish-orange rosettes of ill-defined crystalline structure, with occasionally a few rosettes of needles, or orange-red spheres.

Gold Chloride in concentrated HCl soon crystallizes, forming two kinds of crystals: dark dense rosettes of needles, and round yellow spherical crystals suggestive of yeast-cells, often in circular or spherical clumps. Gold chloride (ordinary chlor-auric acid) slowly forms a few of the latter kind of crystals. Gold bromide in concd. HCl crystallizes gradually in dark dense rosettes of needles and orange-red "yeast-cell" crystals.

IV. Mercuric Chloride Crystals.

Chloromercuric acid and Mercuric sodium chloride give dense brownish rosettes of branching needles or threads in solutions 64 to 8; jagged and blade-like plate crystals form soon in solutions 4 and 2, some branching and some in rosettes.

$HgCl_2$ with the acetate of heroine gives blade crystals in rosettes or branching; with the hydrochloride the results are more like those with chloromercuric acid or mercuric sodium chloride.

The mercuric bromide reagents corresponding to these chloride reagents will give fairly good crystals, rosettes of branching needles and threads, when used with the hydrochloride of heroine, but crystallization is very slow.

V. Platinum Chloride Crystals.

The test with platinum chloride has been a favorite with the chemists of this bureau, even though Stephenson gave first place to $HgCl_2$ and second to Na_2CO_3. Crystals are formed most readily near the limit of precipitation (about 1:400). They are rosettes of needles, suggestive of cockleburrs. There are also spheres; these often form first and change into the rosettes of needles. Under certain conditions the crystals may become plates in rosettes. Platinum chloride & HCl gives similar crystals with more formation of the spheres; the added HCl is not advisable in most cases.

VI. Crystals With Organic Reagents.

Picric acid soon forms crystals in all solutions down to 1. They are dark rosettes of ill-defined crystalline structure or brownish fern-

like rosettes. These rosettes form first as yellow circles or spheres. Stephenson mentioned crystals with picric acid but greatly undervalued it as a reagent for heroine.

Sodium picrate forms brown rosettes of threads in all solutions, 64 to 1 (1:1600). Crystals are formed a little more rapidly than with picric acid.

Alizarin sodium sulfonate gives brownish-yellow spheres or round rosettes of ill-defined crystalline structure in solutions 64 to 8.

VII. Crystals of Free Heroine.

Na_2CO_3, NH_4OH, KCN, borax, or Na_3PO_4 may be used to set free the heroine, which soon crystallizes. NaOH also frees the base but if in any considerable excess very soon dissolves the precipitate by causing hydrolysis to morphine. Heroine is too strong a base to precipitate with K_2CrO_4, Na_2HPO_4, or concentrated potassium acetate. The crystals generally form as plates, usually pointed, in rosettes. There may also be good-sized cubes, etc., as described by Stephenson for KCN. Na_2CO_3 is probably the best basic reagent for heroine, followed by borax or Na_3PO_4. This is the least sensitive of the valuable tests for heroine.

Conclusions

On the basis of both sensitivity and ready formation of characteristic crystals the best tests are probably those with HgI_2-HCl or a similar reagent, Gold chloride in concd. HCl, and Sodium Picrate.

Preservation of Anæsthetic Ether With Hydroquinone—A method put forward for preventing the oxidation of ether consists of the addition of a trace of hydroquinone. The author suggests ½ grain, "a very small pinch," to 4 ounces of ether, and considers that excess of this quantity is harmless. A white half-filled bottle of ether containing a trace of hydroquinone was exposed during six months to diffused light with occasional sunshine, and no peroxide was formed. A control gave a strong peroxide action. This use of hydroquinone is an extension of Moureu's work on the anti-oxidant catalytic action of aromatic hydroxy-compounds, especially those having two hydroxyls in the *ortho-* or in the *para*-position. Those with the hydroxyls in the *meta*-position are much less active; hence the relative inefficacy of resorcinol.—H. O. Nolan (*Lancet,* 1933, 5733, 129).

IS GALENICAL PHARMACY A SCIENCE?*

By Professor A. Tschirch
Berne, Switzerland

ON SEVERAL occasions I have been asked, especially by my German colleagues, what I had in view when I established a galenical laboratory in the new Pharmaceutical Institute in Berne; if it were intended to take away the teaching of prescription filling and the making of pharmaceutical preparations from the practical pharmacist as has already been done, according to my suggestion with the teaching of Chemistry, Physics, and Botany? In other words, did I intend to neglect the American methods in which the prospective pharmacists are taught to fill prescriptions and make preparations in the pharmacy colleges?

I shall therefore try to explain the idea of this innovation, inasmuch as the new Swiss regulations of studies which are not as yet in force accept the course of galenical pharmacy in the prescribed curriculum. I have proposed to introduce in the outline for the Swiss Medical Examinations as the third prerequisite, lectures entitled, "The Scientific Bases of the Preparation and the Various Forms of Medicinal Products." (Galenical Pharmacy.)

The expression, "The Scientific Bases of Galenical Pharmacy," is the title of a short article written by the author which appeared in the *Pharm. Centralhalle,* 1925, No. 34 (in French in *Pharm. Acta Helvetiae,* 1926). This article clearly explains what is intended.

A distinction is made between the practical work in the pharmacy covering which an examination is given (Assistants' Examination), and the studies at the University, in which, besides the lectures concerning the scientific bases of galenical pharmacy, laboratory work in a galenical laboratory at the University is required. The examination, after these studies, consists not only of a practical part covering galenical preparations, but also an oral examination on "the scientific bases of the preparation and production of medicines."

The carefully chosen expression, "scientific bases," leaves no doubt as to the idea of these courses. We do not want to transfer the teaching of practical pharmacy to the university; that shall stay without any restrictions where it is now and the assistant's exam-

*A Translation from the *Apotheker Zeitung* Nr. 4, 1933, done by Kurt Steiger.

ination shall determine whether an assistant is able to fill prescriptions and make preparations.

What now are these scientific bases? Do they already exist, or is it the task of this new department to create them. Many have already occupied themselves with galenical pharmacy, as to how it may be named embracing this whole new branch of study; galenical pharmacy itself meaning only the preparation of medicinals. In Switzerland, Golaz, Siegfried and Büchi have worked on several phases of galenical pharmacy. In Germany, too, one finds from time to time this and that problem sailing under the flag of "animation of galenical pharmacy." I select at random several names like Stich, Rapp and Koerber. Even a plan for a course in galenical laboratory work was once outlined by Casparis and Häfliger.

The fact that most of these works were undertaken in order to improve formulas in the Pharmacopœias makes obvious that their purpose was, in the first place, the utilization of scientific results for the routine work and practice in the pharmacy. All these endeavors are of great value as single studies but there is a lack of a general major idea, and that was the reason why physicians, pharmacists and professors of medicine asked me again and again the question, "After all does there exist a science of galenical pharmacy?"

What is this science? Who invented it? No less men than Aristotle and Hippocrates. "God-like is the doctor who is a philosopher," writes Hippocrates. Aristotle reasons exactly the same for all branches of knowledge. The sign of pure science is, if we look at it in a quite abstract manner, really pure philosophy, *i. e.,* "without any relationship to the routine of everyday life." This is the case in Theology, Philosophy, Philology, Archæology and History. We may thank Aristotle that he invented science because he created through it culture and showed that besides eating, drinking, ploughing and business we have something higher to think about and do.

But in Medicine and Natural Science it is impossible to separate pure science from the practical. And this is the meaning of the great physicist, Helmholtz', words, "Learning alone is not the only object of man in the world. The learning must be applied in life." Thus he describes and justifies, both briefly and well, applied natural science and medicine. On the other hand the chemist, A. W. Hoffmann, stated that "Every fact, which was explored in a serious search of truth, however far it may seem to be from any possibility of practical use, sooner or later will be of value to accomplish the tasks of life."

Who thought that one of the greatest discoveries of Scheele, glycerin, would later form the most important basis in the explosive industry; that formaldehyde, discovered by A. W. Hoffmann, would yield us innumerable medicines and plastics, or that acetanilide, discovered by Gehrhard, would become the type of a whole class of chemical medicaments. The discoverers and inventors certainly did not foresee the future of their products. As to the science of galenical pharmacy that is quite different. Here we are handling the problem from the beginning with the purpose of getting useful results not only for the improvement of galenical preparations themselves, but also as a general restorative for the neglected pharmacy laboratory. The pharmacist may start again with his laboratory work, may make, himself, his own preparations. He will understand the whole process, know why he must proceed in an exact manner, and he will see that his own preparations are as cheap or cheaper and fully as good as preparations from factories. Furthermore, he will know exactly what he dispenses.

What is the meaning of science? It is not science at all if one makes from time to time some experiments to learn a better formula for an extract or a tincture and to start a few days later on an entirely new problem. Science means systematic work on well-considered problems; clear plans and principles in all experiments and observations. And here we find that a galenical science must be created, even if there does already exist a great deal of valuable individual work.

I will try to outline in a general way as follows how the problem may be approached.

As physics and physical chemistry are prevailing in our time the physical and physico-chemical problems may first be emphasized: in the first branch the factors; time, temperature, pressure, light, air, dilution, degree of dispersion, adsorption and absorption; in the second, content, hydrogen ion concentration, chemical incompatibilities, sterilization, influence of humidity and enzymes, and as a biological question the time of drug collection. These are some suggestions, yet they already propose hundreds of experiments for one single tincture and then hundreds of thousands considering all the preparations of a pharmacopœia.

Time is a very important factor in many different respects. First for the extraction and then for the evaporation of the extract in which cases time must be exactly measured. The ageing of tinctures should also be studied, a thing which has not as yet been done. We

all know the beneficial influence of ageing on wine, cognac, cologne water, and so forth—that, for instance, the bouquet is formed only by an extended storage. I have noticed that Rhubarb Powder develops a better odor the longer it is kept in stock. The case may be analogous for medicinal tinctures where of course generally something other than the odor is the active principle.

And in another respect time is to be considered as an important factor, namely, in which season the drug should be collected and for how long it retains its activity. Here may be said that the expression which is still found often in Pharmacopœias, "Must not be kept in storage for more than one year," and vice versa, is not at all scientific. It originates from the time when the pharmacist himself collected his drugs and threw old material away after gathering the new lot. It does not mean anything in our day because we do not know how long the drug has already been stored at the wholesaler's before the pharmacist received it.

Not only the watch but also the thermometer is one of the most important instruments in modern galenical science. One should not work (dry, extract, evaporate) at about 15°-20° C., but at an exactly fixed temperature. One must realize that the modern Galenic is working with physical methods and therefore all measurements must be exact.

Temperature plays a great part not only in the extraction of drugs on preparing tinctures but also in evaporing the liquid under low pressure in preparing extracts, where it must be measured exactly and not only approximately. All this is true, too, in drying drugs. In this way the new Swiss Pharmacopœia is very modern because it indicates the exact temperature at which Vegetable Leaves must be dried. "At normal temperature" is no scientific expression at all, because "normally" the temperature fluctuates considerably. Some time ago one thought that 15 degrees was "normal," but heating systems have spoiled men and today 20 degrees is the lower limit for a "normal" temperature.

Pressure has been quite disregarded until now. But for exact indications the barometric reading should always be mentioned. According to my experience, differences in pressure do not influence very much work which is done at "normal" pressure, even if they fluctuate between 700 and 730, but variations beyond these limits may cause great changes.

The percolator is an apparatus, in which increase in pressure acts as an important factor. In percolators of small height, we find only little pressure. I once increased the pressure in a percolator by putting on a wide glass tubing and by continuous lengthening of this tube to 8 m. (about 9 yards). I got a great abbreviation of the time of extraction. But that was a rather troublesome procedure, because I had to fix this pipe outside of the house. The experiment can be done much easier and with more exactness by using a pump and a manometer. The reduction of pressure is already used to a large extent in preparing galenical products. It is proved, according to the experiences of the chemical and pharmaceutical industry, that evaporation under low pressure (for extracts, etc.) is absolutely indispensable, for small quantities as well as for large ones—indispensable especially in the field of scientific galenics, because it is possible to measure it exactly. And probably the vacuum distillation will be used from time to time.

Both increase and decrease of pressure have been largely used for a long time in the pharmaceutical-chemical laboratories; and they will be still more used in the galenical laboratories.

Light has long been acknowledged as a very important factor. *"A luce remotum"* stands already in old pharmacopœias, written in Latin. But only lately this matter was carefully studied. One knows now that even where no influence of light is visible, for instance, on fats and volatile oils, that even here the light is the cause of deep alteration, and not only the direct sunlight but also diffused light, especially on longer exposure. In this case we have to combine both time and light, and this will naturally be done, because we are forced by our method of measurement to combine the quantity of light with the time of exposure. I stated once in a speech concerning the new Swiss Pharmacopœia—(it may sound very paradoxical)—that the whole pharmacy should be kept in a dark place. This statement is based upon observations, and these observations led to the requirement that a large number of drugs and preparations of the P. H. V must be kept in a dark place, and that often even greater protection from light is required.

On the other hand the light may have a good and desirable action —as in transforming ergosterol into a vitamin; it can act even as à preservative, for example on ferrous salts. The combination of time and light is of unusual importance. A short irradiation may be more

favorable (or harmful) than a longer one. It is doubtful that light is always and under all circumstances harmful, at every length of time, at every concentration and at every temperature. The different parts of the spectrum act probably in different ways. The irradiation with filtered light—here again is to be opened a tremendous field—lead already to very important results, and will lead further to others also in galenical pharmacy, where these experiments are not as yet begun. On this part alone of the new science I see thousands of determinations.

How far and to what importance the quartz-light and fluorescent microscope may become in the field of galenical pharmacy cannot be said. Initially they have been overestimated, as used for the differentiation and diagnosis of foods and drugs. But now, as we learn the limits of their use, it is obvious that they may render a very useful service. Polarization and spectrum analysis, also, though scarcely used to control galenical preparations, are in their way useful. But dispersed, filtered and polarized light are certainly of value, especially in combination with other methods of analysis. The P. H. V makes use of the polarization microscope for the examination of ground drugs. It renders excellent service for that purpose.

The influence of the air must be taken in consideration, which is generally called autoxidation (better maybe, air oxidation). I proved some time ago by a great many experiments (together with Barben), that the rancidity of fats and oils can be considered as a process of autoxidation, in which air-oxygen, light and water are acting all together, taking certain double bonds between central c-atoms as a point of attack. These are the points where the great molecule is breaking into smaller parts. I have many reasons to believe that other substances, too, for example such as resins and volatile oils undergo a similar change. It has been known for a long time that the air has a great influence on the decomposition of caoutchougutto and getahgutta, *i. e.,* the carbohydrates of caouchouc and guttapercha. Every pharmacist keeps his guttapercha-rods under water. We must believe that the molecule of the caouchougutta and the getahgutta, which are the constituents of the proto resins, are unusually large (referring to Standinger). The Teleuto resins, autoxydation-products, resulting from the exposure to the air, bearing the group name of "Albane" and "Fluavile" have much smaller molecules, and are probably products of decomposition by oxydation of the original molecule.

Here again we have a new series of experiments, combining the factors light, time and air, which can be multiplied by the addition of another factor: moisture.

The autoreduction, as I call the reverse process of the autoxydation, which must be taken in consideration for the explanation of the phenomenon of adipocere and hay-stack-fires, is of less importance for galenical preparations, because the isolation from the air is in no case required, and in practice hardly possible to accomplish. Nevertheless some cases are known, for which the autoreduction is probably responsible; for instance, the musty odor of leaf-drugs, kept in hermetically closed containers or the change in color of litmus tincture, which has no contact with the air, and the explosion of chlorinated lime in containers in a hot place, which I believe to be an oxygen explosion. Perhaps the appearance of the fine flavor (bouquet) in old bottled wine is an autoreduction process.

The newest branch of chemistry, which may be called morphological chemistry, explains many phenomena by the form, size, shape and degree of dispersion of the particles, which are engaged in the reaction. Colloid chemistry is based upon these morphological principles. We distinguish now between molecular dispersion, for instance emulsions, which name was taken over (as is known) from pharmacy (but this should not be said to chemists, because they will not admit that chemistry mainly originated and started from pharmacy!).

A long time ago, pharmacists knew that mucilage of acacia was not a true solution; a long time ago the dialysator, which makes use of the outstanding discovery of Graham, concerning the different behavior of crystalloids and colloids towards a semi-permeable membrane—was employed in pharmaceutical laboratories; a long time ago one knew that the degree of dilution of simple homogenous liquids, and, in a coarse morphological field, the degree of diminution have a great influence on that which is generally called the "yield" of the drug. Combining the degree of diminution of the drug and the degree of dilution of the menstruum we get many new series of hundreds and hundreds of experiments, even if we disregard temperature, pressure, time, light and air.

One sees what has to be done in order to create merely a sound basis for a science of galenics. I expect very good results from the requirements for determining viscosity. In this case the new Swiss Pharmacopœia was again a pioneer. And this elegant and beautiful

method will not only prove its usefulness for pharmaceutical chemistry and pharmacognosy in discovering adulterations, but also in the scientific galenical pharmacy.

Much is to be expected from capillary analysis, results from which already prove its usefulness. Nevertheless, it seems to me, it should be combined with two other methods, namely, spectral analysis and chemical reactions. One should cut the strip in different zones, and these should be analyzed separately, which was done once by one of my students in the research department of my laboratories (Pharm. Institut, Berne) with pigments of flowers (published in *Festschrift, Tschirch*).

There is one peculiar phenomenon to which pharmaceutical science paid attention only a short time ago, namely adsorption. The process of adsorption is not yet thoroughly explored and understood, neither from the physical nor from the chemical viewpoint. We do not know yet in our days whether adsorption is combined with chemical reaction or not. That is certainly very unusual, because the whole textile industry, the dyeing of fibres is based upon this process of adsorption. This phenomenon seems to be a morphological problem, a colloidal problem, because the animal fibre, which takes the dye very easily, is to be considered as a colloidal albuminoid, while the cellulose fibre, which generally cannot be dyed directly, has a crystallic structure. Also the fact that it is difficult to extract the alkaloids completely from a very finely ground drug, indicates that there are other problems in this line. In this case also the permeability and the swelling of the drug are obviously important factors.

Here we have a series of the most important physical problems, but there are a great many chemical ones, too. I call your attention only to the great importance of the hydrogen-ion-concentration, chemically, biologically and pharmacologically. We must introduce pH determination into the requirements for the studies of our practical pharmacists, because it is not any more only a pure scientific method.

Great is also the influence of moisture. We have already discussed water as a factor of reaction on the explanation of the rancidity. But of course that is not the only example; there are hundreds more. In the field of drug conservation the lime box creates a new era. The drug, kept on quicklime, keeps its efficiency for unlimited time, because the deteriorating reactions can only go on in the presence of water. Therefore already the old P. H. IV requires that many drugs and preparations be kept over quicklime! Here we find

the junction of Pharmacy and Pharmacognosy. In connection with the water content are the enzymes, which are doubtless in most cases the cause of the deterioration of the active principles of drugs, which takes place in the presence of water, and again in connection with those processes is the so-called stabilization of the killing of the enzymes in the fresh drug, and its reverse, "the preparation of tinctures from the fresh plant," which is required for the homœopathy. One should know that there are three, also pharmacologically, different preparations: the tincture, from the fresh plant, containing all enzymes; the tincture from a drug, containing more or less inactivated enzymes, depending upon the drying temperature; and the tincture prepared from a stabilized drug—that is, a drug heated to more than 60° C. or treated with hot alcohol vapors—which is free from any enzymes. In order to have clear, uniform conditions one should heat all tinctures to the boiling point, because it is obvious that tinctures containing enzymes undergo a deterioration on longer storage. The whole question must be examined pharmacologically, because it is not sure at all that the tincture from the fresh plant is the most effective. We cite a case in which even the fermented drug is the more effective—the gentian root.

These are some of the chemical methods used in scientific galenical pharmacy. And all efforts to check whether light, air, water, degree of dilution of the menstruum, or dispersion of the drug, influence the value of the preparations can only be conducted by chemical means. We determine the acid number, the alkaloidal content, the yield of extracts and so on.

Also in prescription work we are using specific chemical means. The field of incompatibilities, which covers a great space in the new Swiss Pharmacopœia, is, even considering only chemical incompatibilities and disregarding all chemical-pharmacological incompatibilities, so tremendous that it needs still lots of work to fill this gap. But for the physician the pharmacological incompatibility is still more important than the chemical one. According to the rule of Bürgi, the addition of a substance cannot only exert a cumulating effect but also a compensation or an absolutely different or even opposite effect.

Looking over the whole situation, we see that the work is already started in many parts, that in certain points already a great deal of work is done: but we need to get system in this work, clear questions and problems, and we must leave little qualitative experiments and begin with exact, quantitative measuring. Only then galenical pharmacy becomes a science, which is worthy to be taught beside phar-

macognosy and pharmaceutical chemistry in laboratories of the universities and to be used in well-equipped pharmacy laboratories, which is able to bring new life in the pharmacist's laboratory, and which gives to the pharmacist new confidence and enjoyment to prepare for himself his own products.

And that will conduce to a closer contact with the physicians, to the advantage of both of them. It is the great merit of the chief pharmacist of the pharmacy of "Kantonsspital" in Lausanne, Professor Golaz, to show what is practical coöperation between physician and pharmacist. I have contended at the Thoms celebration in Berlin that the phrase, *"Bonum voluisse sat est"* is nonsense. It does not help a great deal to want the good. One must do it, and overcome all obstacles. Golaz started from the very good idea that doctors can only be stopped from prescribing patent medicines by continuous advice and by showing them equivalent preparations made in the pharmacy. Through permanent untireable work, Golaz made, after consulting the physicians and their wishes, preparations and combinations which fulfilled the same purpose as patent medicines. And if those were not quite satisfactory, he made new experiments. I followed these efforts with the greatest interest and I noticed with satisfaction that this coöperation between pharmacist and physician is a really ideal solution of that problem. That goes parallel with my efforts to connect the departments of pharmacy of the universities with the school of medicine, which is already done at the University of Berne. The faculty of medicine was unanimously opposed to the attempt to put the department of pharmacy into the school of philosophy. I am going so far to say that if a university has a department of pharmacy it must belong within the school of medicine, because that is the *only* place where its work can be successful.

In this way the creation of a galenical science receives a much deeper significance and a much greater importance. It creates a broader coöperation between physician and pharmacist, which is for the benefit of both of them and especially for the benefit of the patient, and it forms, through its start of a great effective and loyal fight against worthless patent medicines, the beginning of progressive era in pharmacy.

All pharmacists should follow the example of the hospital pharmacists, who made this coöperation in many places already true. They could, because they are in much closer contact with the physicians, than the owners of public pharmacies, who must search to get that contact.

Appendix

As an example of how I intend to carry through the above outlined problems, I present a study made by one of my students (Mr. Born) under my supervision.

The stable factors were:

Temperature 20° C.

Time of extraction, 6 hours.

Quantity of menstruum (2:100).

Subjects of variation were:

Alcoholic content of the menstrua.

Degree of fineness of the drug. (Cinchona bark.)

Cinchona Bark

Time of extraction, 6 hours. Determination of alkaloidal content, using 2 Gm. of drug. Temperature 20° C.

Drug to menstruum = 2 : 100.

		Alcohol 60%	Alcohol 70%	Alcohol 80%	Alcohol 90%	Alcohol 95%
0	Very rough cut. Size of mesh 9 min.	0.1014	0.07186	0.06504	0.02932	0.02375
I	Rough cut. Size of mesh 5 min.	0.1350	0.09953	0.08507	0.0477	0.03531
II	Medium cut. Size of mesh 3 min.	0.1822	0.1731	0.1414	0.0738	0.0506
III	Fine cut. Size of mesh 1.5 min.	0.2350	0.2164	0.2157	0.1517	0.1241
IV	Very coarse powder. 15 meshes per 1 cm. Thickness of wire 0.2 min.	0.2341	0.2374	0.23084	0.1767	0.1125
IVa	Coarse powder. 20 meshes per 1 cm. Thickness of wire 0.18 min.	0.2457	0.2416	0.2333	0.1850	0.1450
V	Medium powder. 27 inches per 1 cm. Thickness of wire 0.15 min.	0.20106	0.20194	0.20214	0.1617	0.1352
VI	Fine powder. 37-40 meshes per 1 cm. Thickness of wire 0.08 min.	0.1614	0.1590	0.1538	0.1332	0.1130
VII	Very fine powder. 50-51 meshes per 1 cm. Thickness of wire 0.05 min.	0.2164	0.2189	0.1993	0.1759	0.1704

Result: One obtains the tinctures with the highest alkaloidal content by using 60 per cent. alcohol as a menstruum and a coarse powder (sieve No. IVa of the Swiss Pharm. V)—if the above-mentioned conditions are present.

Temperature 20° C., time of extraction 6 hours, and proportion of drug (cinchona bark) : menstruum = 2 : 100.

In order to determine the alkaloidal content of the tinctures, the assay, proposed for the *Pharm. Helv. V* was used.

Thus it is noted that variation of the time of extraction, the temperature and the quantity of menstruum, in addition to the introduction of different pressures, of the sterilization and irradiation as new variable factors yield many new series of experiments—even if one studies only one drug.

This gives an approximate impression of the tremendous extension which the science of Galenics is going to take in the small field of tinctures alone, if various conditions and drugs are going to be studied. It is obvious that the science of Galenics requires a great deal of exact and very careful work and patience.

Strange Chinese Foods Rich in Minerals—The ways of Chinese cookery may be strange but they are particularly good in providing calcium and phosphorus in the diet, it appears from experiments at Oregon State College. The results were explained to the American Home Economics Association.

The dish chosen for the tests was a typical Chinese one, it was reported by Pik Van Hoh and Jessamine C. Williams. The dish was pork spare ribs cut in small pieces and cooked in a solution of rice vinegar, soybean sauce, salt, and sugar for one hour at a low temperature.

An individual serving of this dish contains more calcium and almost half the phosphorus required in a day's diet, according to a minimum standard.

Most of the calcium and phosphorus were present in the finished dish, the experimenters concluded, as a result of the acid solution used in cooking, which drew these food elements out of the pork bone.—(*Science News Letter*, July 29, 1933.)

REPORT OF THE COMMITTEE ON DRUG MARKET TO THE PENNSYLVANIA PHARMACEUTICAL ASSOCIATION CONVENTION*

AT THE time of the compilation of this report, the pharmaceutical industry is sharing in the immediate benefit of the confident tone prevailing in all business circles. During the whole period of the depression, it has been gratifying to observe that the quality of crude and finished materials has been at a high mark and is at least equal to that of more prosperous times. Economy has been practiced in every line, but it is to the credit of the pharmaceutical profession that it has not been at the expense of quality. This fact should be especially valuable to physicians who are dependent for accurate results and the welfare of their patients on the quality and integrity of the substances supplied on their prescriptions. It is also of profitable interest to the pharmacist because it preserves his ethical and professional status in the minds of the physician and the public whom they both serve. Not one instance of intentional adulteration or of misbranding has been reported by the laboratories contributing to our report.

The usual number of chemicals, oils, spices, drugs, etc., were found to be of sub-standard quality according to the U. S. P., N. F., or other requirements. In fact, R. I. Grantham reports that it was necessary to reject only 63 of the 5,298 lots of pharmaceutical chemicals, alkaloids, volatile oils and other substances examined because of their divergence from the U. S. P., N. F., or other standard. He also offers the following very important observation concerning substances for hypodermic use: "Materials entering into the manufacture of products for hypodermic medication must be of the highest degree of purity obtainable. It is of particular importance that they be free from substance insoluble in water. The Pharmacopœia does not specifically cover this point for these materials. It is not unusual to find alkaloidal salts containing an excessive amount of 'floaters,' particles of dust, filter paper, etc. Several shipments of these basic materials were rejected during the last year because they did not meet with our specific requirement in this respect. These items included: one shipment of Quinine and Urea Hydrochloride U. S. P., five shipments of Codeine Phosphate U. S. P., two shipments of Codeine Sulphate U. S. P., one shipment of Caffeine Sodium Benzoate U. S. P., one shipment

* Bedford Springs, Pennsylvania, June 27-29, 1933.

of Atropine Sulphate U. S. P., one shipment of Sodium Chloride C. P., and one shipment of Lactose."

It is plain that the pharmaceutical and other industries are about to witness considerable change in methods as a result of the legislation recently enacted by the Federal Government. The organization of the National Industrial Recovery Administration is an important step in this direction. In this connection, we submit the following paragraphs by J. Mervin Rosenberger on the past and present trends of business in the drug trade:

"We are pleased to render a report this year in a more confident spirit than that which was prevalent during the last few years. In fact, we are able to report considerable improvement in June business throughout practically every branch of industry, which is due no doubt to the various Governmental measures that have been recently undertaken. The Government by such measures has caused a considerable amount of buying.

"During the previous depressed period practically all buying was done on a hand-to-mouth basis. In almost every instance after the purchase had been made, prices declined to a still lower level. This condition has now no doubt become a thing of the past and there has been a decided upward price tendency.

"As soon as the Government adopted inflationary measures prices immediately advanced, especially on imported materials. In the drug and chemical field the first items to be affected were the essential oils. Just as rapidly as the American dollar declined in the foreign market, the prices of foreign crude materials were advanced accordingly. In reading the various drug journals, previous to this time, you will note that every issue contained numerous declines of all drugs, chemicals, essential oils and other druggists' supplies with virtually no advances. Today this condition is reversed and there are now numerous advances, with very few declines in prices.

"It is also of interest to know that a bill has been presented to Congress repealing the Food and Drugs Act of 1906 and substituting an entirely new law much lengthier and broader in scope. The department lists the most important provisions of the bill, as follows:

(1) Prevention of false advertising.

(2) Inclusion of cosmetics.

(3) Establishment of tolerances for poisons in foods.

(4) Authority to establish standards for foods.

(5) Power to require producers to secure permits in certain cases.

(6) Establishment of current medical opinion as the basis for ruling on therapeutic claims of drug products.

(7) Requirement of more informative labels.

"The formation of the Drug Institute of America will perhaps have an outstanding effect upon the Drug, Pharmaceutical and Chemical industries in the very new future.

"In addition to the optimistic report in the Drug and Chemical industry, conditions are very much improved in practically every other industry and we feel that in the near future business conditions in this country as well as abroad will be greatly improved."

Among the substances of sub-standard quality were Arsenous Iodide U. S. P., Calcium Lactate U. S. P., Calcium Phosphate N. F., Magnesium Carbonate U. S. P., Sodium Citrate U. S. P., Sodium Phosphate U. S. P., Oil of Rosemary, Oil of Anise, Oil of Cassia, Oil of Sandalwood, and Oil of Cod Liver. These did not comply with the U. S. P. or N. F. standards in various particulars.

One shipment of Calcium Lactate was rejected because of an excessive amount of volatile fatty acids. Two samples of Acetanilid had offensive odors, and did not comply with the U. S. P. melting point requirement. In addition, there were two shipments of Bismuth Subcarbonate U. S. P. that contained an excess of nitrates, five shipments of Phenol having a pink color, one of which had a melting point far below the U. S. P. standard, and a sample of Tri-Sodium Phosphate with an excess of chlorides.

Other interesting items were a shipment of Lard U. S. P. which was rejected because of discoloration and an offensive odor, and a shipment of Benzoinated Lard U. S. P. which was dirty. A sample of Glycerin had a low specific gravity which indicates either improper distillation or of dilution.

One shipment of Compound Solution of Cresol U. S. P. did not comply with the U. S. P. requirements with respect to the boiling point of cresol. A lot of Oil of Orange was rejected because of cloudiness; it had evidently not been properly purified. An excessive amount of water was present in each of five shipments of Soft Soap U. S. P. examined. One sample was offered which did not comply

with other U. S. P. standards. The rejection of five shipments of Wool Fat Anhydrous was required because they did not meet the U. S. P. requirements for melting point. They were quite soft at room temperature but did not show evidence of the presence of other fats or paraffine. This is apparently a grade of wool fat not previously seen on the market. Samples of Solution of Sodium Glycerophosphate were found to contain excessive amounts of phosphates, and as in previous reports, we again report Castile Soap with a low iodine number.

The quality of spices has been up to the usual standards. One laboratory reports that all samples of Allspice, Cloves, Coriander, Nutmeg, White Pepper and Black Pepper examined were of good quality. One sample of Cinnamon and eight samples of Mace were rejected because of a high acid-insoluble ash content. Two shipments of Ginger contained an excess of Lime.

As usual, the Food and Drug Bureau of the U. S. Department of Agriculture has very closely examined importations, and items not meeting their standards have been rejected. Many importations of seeds such as Anise, Caraway, Celery, Cumin, Fennel and Mustard were rejected because of filth or an excessive amount of ash. Several lots of other spices such as Mace and Nutmeg were rejected for the same cause or on account of having been worm-eaten.

The alkaloid containing drugs were generally satisfactory with but few exceptions, such as several shipments of Stramonium Leaves having an excess of acid-insoluble ash, and a shipment of Nux Vomica that was deficient in alkaloids.

The following table gives results obtained in the analyses of various spices:

Name	Total Ether Extract	Volatile Oil	Water Extract
Allspice	9.10%– 9.25%		
Cinnamon		2.40%– 3.60%	
Cloves		16.30%–18.50%	
Coriander Seed ...	19.00%–20.25%		
Ginger			12.00%–14.00%
Pepper, Black	7.65%– 9.50%		

Jos. W. E. Harrisson.

Physiological assays of crude drugs during the period June 1, 1932, to June 1, 1933, have shown results given in the following table:

Product	Total Number Samples Assayed	Number Samples Between 90% & 110% of U. S. P. Requirement	Range of Potency
Aconite	8	2	150–153%
Cannabis	5	5	90–100%
Ergot	20	0	120–180%
Digitalis	31	16	77–137%
Strophanthus	4	2	40–108%
White Squill	25	12	54–135%
Red Squill	1	1	94%
Total	94	38	40–180%

James C. Munch, Arnold Quici.

Reporting on galenicals, Jos. W. E. Harrisson reports the examination of numerous samples, "many of which were being supplied in package form to the retail pharmacist. Of these, Tincture of Iodine, Sweet Spirits of Nitre, Spirit of Camphor, Liniment of Camphor were in many instances below standard. Certain proprietary products also were found not only to be adulterated, but in some instances, packages, labels and contents were counterfeited. It is well then for the retail pharmacist to make purchases only from established pharmaceutical houses who have earned the confidence of the profession."

The committee presents this report with the confidence that it contains information of value to our members, and hopes that it will help to maintain the scientific prestige which our Association has so capably earned.

We also wish to acknowledge our indebtedness to the staffs of the analytical laboratories of Sharp & Dohme, LaWall & Harrisson, and the Smith, Kline & French companies.

Submitted June 27, 1933.

J. G. Roberts, Chairman,
J. Mervin Rosenberger.
R. I. Grantham,
Jos. W. E. Harrisson.

A COLLABORATIVE COMPARISON OF FIVE OPIUM ASSAY PROCEDURES

By A. Richard Bliss, Jr.,* E. D. Davy, Joseph Rosin,† W. H. Blome ‡ and R. W. Morrison §**

ALTHOUGH it is true that most investigators in the United States have raised no serious criticisms of the U. S. P. X procedure for the assay of opium,[1] some objections have been raised against the U. S. P. method,[2] and among them are: (a) the procedure gives too high results; (b) the procedure gives too low results; (c) it requires too much time; (d) it requires too much opium. When some of the data obtained by the International Committee on Opium Assay Methods of the League of Nations became available, it seemed desirable and important that some collaborative, experimental work be done with a number of the more promising methods studied by that Committee, and that a comparison be made with the U. S. Pharmacopœia method since it appears that the U. S. P. X method was not considered by the League of Nations Committee. Accordingly, portions of the same lot of drugs were subjected to the following assay procedures:

1. Rosin's Method.[3]
2. The Method of Eder and Stucki.[4]
3. Rusting's Modification of the Netherland Pharmacopœia Method.[5]
4. The British Pharmacopœia Method.[6]
5. The U. S. P. X Method, *modified by using the Jena glass filtering funnel.*[7]

The Procedures

1. *Rosin's Method.*—Triturate in a mortar 6 Gm. of the opium which, if fresh, should be in very small pieces, and if dry, in a powder, with about 40 cc. of water for 15 minutes. Transfer completely into

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a flask with the aid of 30 cc. of warm water, stopper the flask and let stand for *one hour,* shaking every 10 minutes, or continuously in a mechanical agitator. Pour the contents as evenly as possible upon a wetted filter of 10-11 cm. diameter or, preferably, upon a glass funnel with a sintered glass bottom attached to a suction flask. When the liquid has drained off, wash the residue with about 20 cc. of water, carefully dropped upon the edges of the filter and its contents. Transfer the moist residue into a mortar, rub it to a smooth paste, then rinse it into the original flask with 40 cc. of water, agitate thoroughly for 10 minutes, and return the whole to the filter. When the liquid has drained off, wash the residue with small portions of water until the washings run nearly colorless. Evaporate the filtrates and washings in a *tared* dish to about 30 Gm. and allow to cool. Add 3.0 Gm. of freshly slaked lime, triturate for 15 minutes and transfer completely into a *tared* flask with the aid of small portions of water; add sufficient water to make 54 Gm., and mix well. Filter through a dry filter of 10-11 cm. diameter into a dry cylinder or small flask, inserting the funnel in the neck of the receiving vessel and keeping the funnel covered with a glass during filtration.

Place 34 Gm. of the filtrate (corresponding to 4 Gm. of opium) in an Erlenmeyer flask of suitable capacity, add 2 cc. of alcohol and 15 cc. of ether, and after shaking the mixture add 1 Gm. of ammonium chloride. Stopper the flask, shake it frequently during 10 minutes, and set aside in a cool place over night. Remove the stopper and brush any adhering crystals back into the flask. Decant the ethereal layer through a small filter paper. Rinse the flask and contents with 15 cc. of ether and pass it through the filter, washing the filter with an additional small quantity of ether. When the ether has all drained off, pour the aqueous layer onto the filter without trying to remove the crystals. Wash the crystals in the flask and contents of the filter with distilled water until the washings are colorless. Add to the precipitating flask about 10 cc. of hot neutral methanol, agitate to dissolve as much as possible of the morphine in the flask, and pour the solution over the morphine on the filter, receiving the filtrate in a suitable flask. Repeat this treatment with hot methanol three or four times, using 5-7 cc. each time, until all of the morphine has gone into solution. Cool and add an accurately measured volume of 20 cc. or 25 cc. of N/10 sulphuric acid. Dilute the solution with 50 cc. of

water and titrate the excess of acid with N/10 sodium hydroxide using methyl red indicator. Each cc. of N/10 acid consumed corresponds to 0.0285 Gm. of anhydrous morphine.

2. *The Method of Eder and Stucki.—The Determination of Morphine in Opium:* Dry about 1 Gm. of opium powder, accurately weighed, for two hours at 103-105° C., weigh and dry again for one hour periods until the additional loss of weight does not exceed 0.005 Gm. Triturate 0.50 Gm. of opium powder (V) with approximately 2 cc. N/1 hydrochloric acid to a uniform paste, rinse into a tared Erlenmeyer flask with N/1 hydrochloric acid and add sufficient N/1 hydrochloric acid to make the combined weight 10.25 Gm. Shake repeatedly and vigorously during one-half hour. Filter as much as possible of the acid extract into a tared dish and weigh. Evaporate on a steam bath to dryness, and dry the residue at 103-105° C. until the loss of weight, after one hour additional drying, is not more than 0.03 Gm. Weigh the dried residue after cooling and calculate the percentage (x) by the following formula:

$$x = \frac{m\,(1950\ \textit{plus}\ y)}{p\ \textit{minus}\ m}$$

where

y = moisture content of opium in per cent.
p = weight of opium in grams.
m = (weight of the) residue p, expressed in grams.

Determination of Morphine Content: Triturate 1.30 Gm. of opium powder (V) with approximately 2 cc. of N/1 hydrochloric acid to a uniform paste, transfer with the aid of N/1 hydrochloric acid into a tared medicine bottle of 50 cc. capacity, and make up with N/1 hydrochloric acid to a total weight of

$$\frac{27.3\ \textit{minus}\ (x\ \text{plus}\ y) \times 1.3\ \text{Gm.}}{100}$$

Shake the mixture vigorously and frequently during one-half hour and filter through a filter 7 cm. diameter. Transfer 20 Gm. of the filtrate (equivalent to 1 Gm. of opium powder) into a separatory funnel of 125-150 cc. capacity, the stopcock of which has previously been moistened with water (not greased with fat or petrolatum), add 30 cc. of chloroform-isopropyl alcohol mixture (3 vol. plus 1 vol.),

shake quickly and add dropwise, while agitating, 2.5 cc. of concentrated sodium hydroxide solution (10 N) and shake well for two minutes in order to extract all by-alkaloids. After separation of two layers, transfer the somewhat turbid chloroform-isopropyl alcohol layer into a second similar separatory funnel. Repeat the extraction of the alkaline solution twice with the chloroform-isopropyl alcohol mixture. Then shake the combined chloroform-isopropyl alcohol extracts in the second separatory funnel with 10 cc. of N/10 sodium hydroxide solution in order to remove any dissolved morphine. After separation of the layers, draw off the still somewhat turbid chloroform-isopropyl alcohol layer and shake the 10 cc. of N/10 sodium hydroxide remaining in the funnel with 20 cc. of ether for 2 minutes in order to remove the last traces of by-alkaloids.

When the layers have separated and become clear, combine the N/10 sodium hydroxide solution in the first separatory funnel, add 60 cc. of chloroform-isopropyl alcohol mixture and 0.6 Gm. of ammonium sulphate, shake for one minute and allow to stand for at least 15 minutes. Repeat the extraction twice with 40 cc. of the chloroform-isopropyl alcohol mixture. After the separation of the layers filter the still somewhat turbid chloroform-isopropyl alcohol extracts successively through a double filter of 8 cm. diameter, previously moistened with chloroform, into an Erlenmeyer flask of 300 cc. capacity containing a few glass beads, and rinse the filter with small portions of the chloroform-isopropyl alcohol mixture. Remove the solvent completely by evaporation on a steam bath and loosen the residue from the bottom of the flask by gently warming with 5 cc. of alcohol. Then add 15 cc. of N/10 hydrochloric acid, and dissolve the morphine completely by rotating, but without warming. Dilute with 100 cc. of freshly boiled and cooled water, add 10-12 drops of methyl red, and titrate the excess acid with N/10 sodium hydroxide to the disappearance of the red color (use a microburette).

$$1 \text{ cc. N/10 HCl} = 0.0285 \text{ Gm. } C_{17}H_{19}O_3N$$

3. *Rusting's Modification of the Netherland Pharmacopœia Method.*—Carefully triturate 2 Gm. of powdered opium with 2 cc. of water to a perfectly homogeneous mass, gradually dilute with 20 cc. of water, dissolve in the mixture 500 mgm. of manganous chloride, and then mix with it 1 Gm. of calcium hydroxide. After a few minutes the mixture is transferred to a filtering tube (*e. g.*, Jena glass

Buchner Funnel, A. H. Thomas Co. Catalogue No. 5593-3G3), which is inserted in one perforation of a rubber stopper. This stopper is inserted into the neck of an Erlenmeyer flask of about 50 cc. capacity. Through the other perforation of the rubber stopper there passes a suction tube connected with a water pump. The pump is set in operation until the liquid begins to drip. Six washings are now made with 2 cc. of water used each time; the first portions of the washings are used for rinsing out the mortar. The suction should be at first gentle, but toward the end strong, in order to obtain as much filtrate as possible. Channel formation must be avoided. To the filtrate, about 2 cc. in volume, add 15 cc. of ether, swirl for 2 minutes, then add 300 mgm. of ammonium chloride, swirl for 15 minutes more, and then let stand until the next day.

The ethereal layer is decanted, the liquid again swirled with 5 cc. of ether, and this too decanted. Now filter through a folded filter of 2.5 cm. radius, and wash five times with 3 cc. portions each time of a saturated aqueous morphine solution. Dissolve as completely as possible the residual morphine in the flask in 15 cc. of N/10 acid, heat, and pour the solution slowly on the filter until all the morphine has completely dissolved. Wash the flask and the filter with small quantities of boiled water, and until the reaction is no longer acid. After adding 1 or 2 drops of methyl red solution, titrate with N/10 alkali until a color change develops. Then add 2.5 to 3 drops of phenolphthalein solution and titrate with vigorous shaking, until a just permanent red color develops.

The titration with methyl red gives the morphine-calcium meconate; the titration with phenolphthalein gives the morphine alone.

1 cc. acid = 28.5 mgm. anhydrous morphine.

4. *The British Pharmacopœia Method.*—The method employed is that described on pages 316-317 of *The British Pharmacopœia,* 1932.

5. *The U. S. P. X Method, Modified by Using the Jena Glass Filtering Funnel* (Jena Glass Buchner Funnel, A. H. Thomas Co. Catalogue No. 5593-3G3), employed in the Rusting modification method.*

* Suggested by Doctor Charles H. LaWall, of the International Commission.

Observations and Discussion

The collaborators' results are given in the table below.

TABLE I—RESULTS OBTAINED WITH FIVE ASSAY PROCEDURES FOR OPIUM

Analyst	Rosin Meth.	Eder & S. Meth.	Rusting Meth.	B. P. Meth.	Mod. U. S. P. Meth.
A. R. Bliss, Jr.	10.06*	10.72	9.82	10.64	10.18
	10.09	10.45	9.65	10.63	10.15
Averages	10.08	10.59	9.74	10.64	10.17
W. H. Blome	....	....	7.83	10.52	9.764
			2.56@	10.52	10.660
Averages				10.52	10.212
E. D. Davy	9.64	10.83	7.40	10.68	9.70
	9.71	10.26	7.50	10.66	9.87
Averages	9.68	10.55	7.45	10.67	9.79
R. W. Morrison	9.62	10.60	8.63	10.05	9.72
	9.70	10.51	8.72	9.89	9.76
				9.93	
Averages	9.66	10.56	8.68	9.97	9.74
Joseph Rosin	10.10	....	9.83	10.62	10.31
	9.99		10.41	10.62	9.90
Averages	10.05		10.12	10.62	10.11
			9.61@		
			10.10@		
Averages			9.86@		
Grand Averages ..	9.87	10.57	8.76	10.48	10.004

* Figures represent the per cent. of anhydrous morphine. Methyl red was used as the indicator except in the cases of those values marked "@" in which phenolphthalein was employed.

W. H. Blome: "The methods 2 and 3 are extremely long and, in our judgment, none of them are practical because of their excessive length and costliness. If other shorter methods will answer the purpose reasonably well, they certainly would be preferred by manufacturers for several reasons:

"1. The methods (2, 3) recently sent out require an excessive amount of a chemist's time.

"2. They cause the tying up of manufacturing apparatus which may be needed for other purposes over an inordinately long period of time.

"Methods 4 and 5 (B. P. and U. S. P.) appear to be shorter than the others. The checks in the second one were not especially good, but that may be accounted for by the fact that one of the assays had to stand over Saturday and Sunday. In the case of method 4, the two assays checked exactly, the result in both cases being 10.52 per cent. of anhydrous morphine. We would suggest that method 5 is too long, and that our preference is for the B. P. method (method 4).

"In the first paragraph of method 3 (Rusting's modification) we are directed to wash the opium six times with 2 cc. of water at each washing. Our experience has been that this quantity of water is not sufficient to exhaust the opium of its morphine. As the operator is assumed to use his knowledge gained from experience, it stands to reason that he will continue to wash until all the alkaloid has been removed. If this is done, the volume of liquid will be increased over and considerably above the amount stated. In such a case we assume that the volume of the liquid should be evaporated down to the stated volume. Incidentally we may state that one assay was made carrying the washing to completion, but probably because of this volume, the assay appears to be quite unsatisfactory. Carrying the titration only to the end reaction with methyl red as indicator we found but 2.5 per cent. of morphine. With phenolphthalein as indicator the yield undoubtedly would be still less.

E. D. Davy: "The Rosin method works very well and yields concordant results. The Eder and Stucki method is too long and tedious, and certainly no more accurate than when the sample of drug is exhausted with a suitable solvent, the filtrate made to a definite volume and an aliquot taken. In the event the volume exceeds a workable amount it may be evaporated. I am not criticizing the shake-out method of procedure, although in this case some persistent emulsions were formed.

"Rusting's method yielded consistent but low results. The B. P. method works very well, and, when the correction is eliminated, checks very closely with the Rosin and the U. S. P. values. The first part of the B. P. procedure is an improvement over our present U. S. P. method. In 1931 we did some work on opium assays, and incidentally determined the loss of morphine in the aqueous portion. Using 2 cc. of alcohol, 30 cc. of water, and 15 cc. of ether, as in the U. S. P., the loss was 1.55 mgm. per cc., or 0.049 Gm. as compared with the B. P. correction of 0.052, in which they use 5 cc. of alcohol and 52 cc. of

filtrate. Undoubtedly the extractive matter affects the proportion of morphine held in solution."

R. W. Morrison: "The present U. S. P. method, the method of the B. P., and Rosin's method yield the more satisfactory results. The method of Eder and Stucki yielded the highest results, while that of Rusting yielded the lowest. In the case of Rusting's modification method I do not believe that the sample of opium is washed with sufficient water to extract all of the morphine. Further, since there is no time factor given for the trituration of the opium with the calcium hydroxide, this, too, may lead to low results. Although the method of Eder and Stucki does not require the sample to stand over night, I believe that the working time involved in this method is greater than in the others. It is a bit too complicated to be practical. The experimental error is probably higher because of the small amount of opium used in the procedure."

Joseph Rosin: "None of the various assays that have been proposed by the League of Nations are, in my judgment, as satisfactory as the U. S. P. assay. In my own experience the results obtained by the U. S. P. assay are approximately correct, more so, on the average, than by other assays. The U. S. P. assay, however, has a few pitfalls which may cause slightly too high results. The assay I proposed takes care of this. This assay also uses less opium to begin with, although it finishes up with the same amount of opium as in the present U. S. P. Further, which is of some moment, is the fact that it shortens the assay by a whole day, *i. e.,* instead of requiring an interval of three days, as by the present U. S. P., the assay can be performed in an interval of two days, or practically within twenty-four hours. If one starts it at about 10 o'clock in the morning, he should have it finished the following morning at about the same time.

"We have not assayed the opium by method 2. This method calls for the use of 1.3 Gm. of opium, winding up with 1 Gm., and the total amount of N/10 acid consumed is only about 3.5 cc. An error in any stage of the assay will make a large difference in the result. Furthermore, even granting that this method is applicable to opium powder, it would not be satisfactory for gum opium. 1.3 Gm. could not be expected to give a representative sample of gum opium.

"In addition to the assays enumerated, we also tested this opium by the German Pharmacopœia V method, and it is interesting to note that by this assay we found only 8.9 per cent. of anhydrous morphine."

A. R. Bliss, Jr.: "I am rather pleased with the Rosin method, which not only shortens the procedure by approximately a day, but also includes the major advantages of the method of the British Pharmacopœia, and the filtering funnel improvement suggested by the Eder and Stucki method. The values obtained checked very nicely with those yielded by the method of the U. S. P. X, modified, as suggested by Doctor Charles H. LaWall, of the International Commission, by using the Jena glass filtering funnel.

"Although the Eder and Stucki method yields results which check rather closely, it is too long and tedious. The small amount of drug used in this procedure is a handicap in accurate analysis. The aliquot portion feature of this method may also introduce an error.

"The method of the British Pharmacopœia is fairly satisfactory. My major objections are: (a) the correction element—undesirable as a matter of principle in any assay procedure; and (b) the aliquot portion element.

"The long-tried U. S. P. X procedure, modified as suggested by Rosin, is superior, when measured from every angle, to the various methods tried out by the International Commission."

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(4) Private communication from Dr. C. H. LaWall.

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(7) Private communication from Dr. C. H. LaWall.

ABSTRACTED AND REPRINTED ARTICLE

ANIMAL PHARMACEUTICALS OF THE PAST AND PRESENT†

By Charles Whitebread*

THE NATURAL desire which we experience for self-preservation has led mankind, from the earliest ages, to distinguish carefully between those things which minister to health and the prolongation of life, and those which may impair the former and shorten the latter. They have specially directed their efforts to preventive measures, but perceiving that, notwithstanding all their care, they are sometimes taken by surprise and are not able to avoid the causes of injury or disease, they have, as a last resort, devoted their energies to the discovery of remedies and of methods of cure to be applied when precautions have failed.

Seeing that those who died had apparently committed some error which gave to their ailments a fatal character, and that those who survived had made use of certain things, not necessary or desirable in health, to which their recovery was attributable, man was led to avoid the mistakes which proved injurious and to adapt for himself and others the remedies which proved beneficial.**

In the progress of civilization various incidents have gradually unfolded the remedial powers of many natural substances. These were recorded and the authentic history of medicine and pharmacy dates its commencement from the period when such records were begun. The Chaldeans and Babylonians, we are told by Herodotus, carried their sick to the public roads and markets that travelers might converse with them, and communicate any remedies which had been used in similar cases. This custom is said to have continued during many ages in Assyria. It is also said that it prevailed among the ancient Lusitanians or Portuguese. In this fashion the results of experience traveled only by oral tradition.

It was in the temple of Aesculapius in Greece that medical information was first recorded. Diseases and medicines were there

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**Leclerc, *Histoire de la Medecine*.

registered on durable tablets of marble. The priests and priestesses, who were the guardians of the temple, prepared the remedies and directed their application, and thus commenced the professions of pharmacy and medicine.

With respect to the actual nature of the remedies used by the early Asclepiads it is useless to inquire except in a few instances. The

Living Creatures, *&c.* *The Phyſitians Library.* 69

Heart as any is, being beaten into Pouder and taken inwardly; alſo it reſiſts Peſtilence and Poiſon.

The Skull of a Man that was never buried, being beaten to Pouder, and given inwardly, the quantity of a dram at a time in Betony water, helps Palſies and Falling-ſickneſs.

That ſmall Triangular bone in the Skull of a Man, called *Os triquetrum*, ſo abſolutely cures the Falling-ſickneſs, that it will never come again, ſaith *Paracelſus*.

Thoſe ſmall bones which are found in the fore-feet of a Hare, being beaten into Pouder, and drank in Wine powerfully provoke Urine.

A Ring made of an Elk's Claw being worn helps the Cramp.

The Fat of a Man is exceeding good to anoint ſuch Limbs as fall away in the Fleſh.

Gooſe greaſe and Capons greaſe are both ſoftning, help gnawing Sores, ſtiffneſs of the Womb, and mitigate Pain.

I am of Opinion that the Suet of a Goat mixed with a little Saffron is as excellent an Ointment for the Gout, eſpecially the Gout in the Knees, as any is.

Bears greaſe ſtays the falling off of the Hair.

Fox greaſe helps Pains in the Ears.

Elks Claws or Hoofs are a ſoveraign Remedy for the Falling-ſickneſs, though it be but worn in a Ring, much more being taken inwardly: but ſaith *Mizaldus*, it muſt be the Hoof of the Right Foot behind.

Milk is an extream windy Meat; therefore I am of the Opinion of *Dioſcorides*, viz. That it is not profitable in Head-aches; yet this is for certain that it is an admirable Remedy for inward Ulcers in any part of the Body, or, any Corroſions or Excoriations, Pains in the Reins and Bladder; but it is very bad in Diſeaſes of the Liver, Spleen, the Falling-ſickneſs, Vertigo, or Dizzineſs in the Head, Fevers and Head-aches. Goats-milk is held to be better than Cows for Hectick Fevers, Pthiſicks and Conſumptions, and ſo is Aſſes alſo.

Whey extenuateth and Cleanſeth both Choler and Melancholy: wonderfully helps Melancholy, and Madneſs coming of it: opens ſtoppings of the Bowels; helps ſuch as have Dropſies, and are troubled with the ſtoppings of the Spleen, Rickets, and

Fig. 1—Reproduction (red.) of page from Dr. Culpepper's London Dispensatory—gives some idea of the forerunners of organotherapy as practised in England in 1718. (Courtesy of U. S. National Museum.)

lapse of ages, loss of records, change of language, and ambiguity of description have rendered research unsatisfactory. Indeed, we are in doubt concerning many of the medicines which even Hippocrates used.

It is shown by the earliest records that the ancients were in possession of many powerful remedies. Thus, Melampus of Argos, a Greek physician who is supposed to have lived about 1380 B. C., is said to have cured one of the Argonauts of sterility by administering the rust of iron in wine for ten days. The same physician used hellebore as a purge on the daughters of King Praetus who were afflicted with melancholy. Opium, or a preparation of the poppy, was certainly known in the earliest ages.

There are records of ancient magic cures being effected by animal drugs. For instance, a memorial tablet found on the site of an Aesculapian temple records the following among other cures: "A blind soldier named Valerius Aper, having consulted the oracle was directed to mix the blood of a white cock with honey, and make of it an ointment which he was to rub on the eyes for three days. He recovered his sight and went to thank the god before all the people."

The endeavor to find medicinal virtues in parts of animals dates back to time immemorial. Mythology furnishes legends of pharmaceutical interest concerning the fabulous animals, the phoenix, the unicorn, and the dragon. According to Herodotus the phoenix was a bird about the size of an eagle. It was believed to be immortal and was worshipped by the Egyptians. It was adopted by the alchemists as their emblem, and was afterward a sign used by the pharmacists. Aristotle described the unicorn as an animal resembling the Indian wild ass, with a single long horn projecting from the center of its forehead. This horn was a medicine, and the unicorn was a frequent sign used by apothecaries. The dragon was associated with pharmacy by means of the "blood" which at one time was supposed to be yielded by it.

The Papyrus Ebers, a treatise on materia medica, pharmacy, and therapeutics, one of the oldest known medical works, which was believed by its discoverer to have been compiled about 1552 years before the Christian Era, in the time of Moses, and before the exodus of the Israelites from Egypt, contains references to the animal, mineral, and vegetable drugs of that time. Among the animals mentioned are the buffalo, stag, ox, pig, camel, ram, dog, crocodile, bat, goose, tortoise, beetles, and flies. Among the animal substances used as medicines

were blood, human brains, urine, feces, genitals of cats, various animal oils, honey, milk, eggs, and wax.

Hippocrates, "The Father of Medicine" (460-370 B. C.), who practiced about 800 years after the period of Aesculapius, the Greek

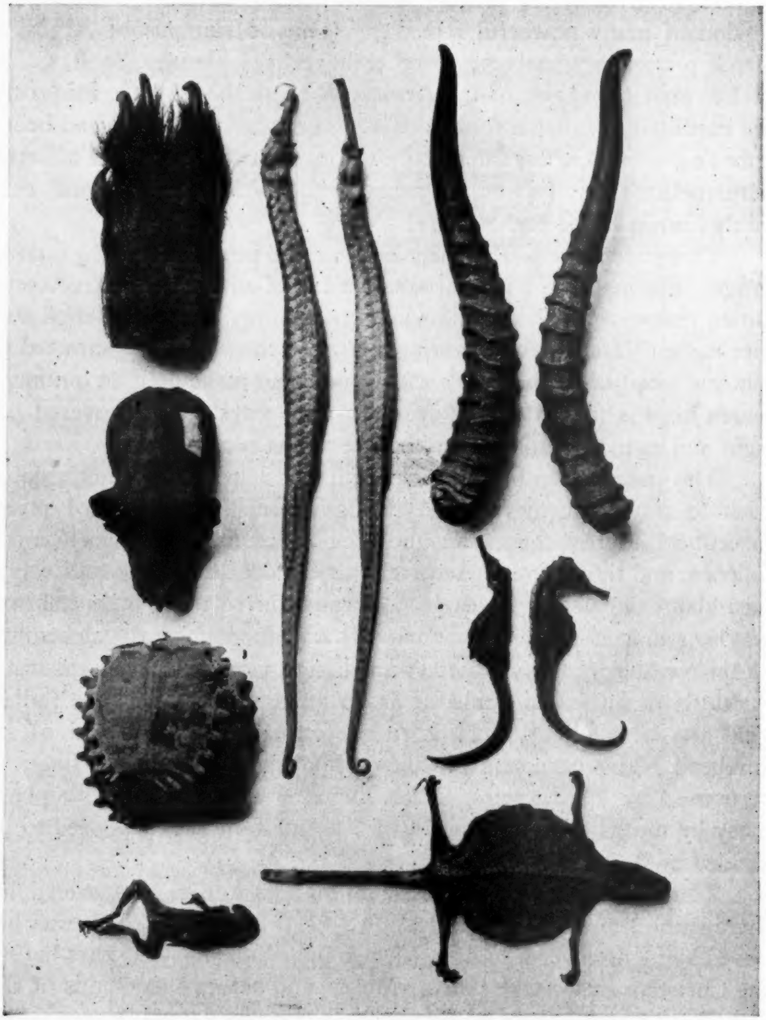

Fig. 2—Animal substances as kept in apothecary shops of the past: 1. (Top left) Bear's claw; 2. (reading downward) charred monkey skull; 3. tortoise shell; 4. dried frog; 5. pipefish; 6. antelope horns; 7. seahorses; 8. lizard. (Courtesy of U. S. National Museum.)

"God of Medicine," mentioned nearly four hundred simples in his numerous writings. These included milks, wines, fruits, and vegetables, as well as other substances, which would be classified with the foods of today. Among the animal drugs of the time of Hippocrates may be mentioned aparine (goose grease), cantharides, centipedes, crayfish, dog, excrement of the ass, goat, mule, goose, and fox, frogs, honey, horns of the ox, goat and stag, ostrich, ox liver, gall, and urine, red spider, serpent, sweat, torpedo fish, turtle, wax and worms.

Between Hippocrates and Galen, called "The Father of Pharmacy," an interval of some six hundred years elapsed. Galen was an enthusiastic admirer of Hippocrates, and used all the power of his genius and the influence of his name to maintain the practice of medicine on the foundation laid for it by Hippocrates in the study of the natural history of disease. Galen's writings and teachings had almost undisputed authority in medicine down to the sixteenth century. It has been estimated that Galen's materia medica consisted of 540 plants, 180 animal and 100 mineral substances. He was a prolific writer on pharmacy, and the preparation of medicines by physical means is still called galenical pharmacy.

It was in the sixteenth and seventeenth centuries that the introduction of animal remedies developed rapidly. From the number of animal substances made official in the London Pharmacopœias of 1618, 1650 and 1677, it would seem that the world was ransacked for animal medicines with which to alleviate human ills. Illustrations of apothecary shops of that time usually show a crocodile suspended from the ceiling, and different animal carcasses in other parts of the store. The animal pharmacy of this time, which was practiced in all countries, continued in some parts of the world on an extensive scale till about fifty years ago. It is not practicable to list many of these materia medica specimens, but striking examples of some of those retained in the collections of the United States National Museum and now on exhibition in the Division of Medicine will serve to illustrate this phase of the medicine and pharmacy of bygone days.

ANTELOPE HORNS. The horns of the goat antelope, *Ncmorhoedus crispus*. Used, in coarse powder or partially calcined, in cerebral affections and rheumatism, and especially in the various diseases accompanying pregnancy. The shavings, said to be a cooling medicine, were supposed to cure inflammation of the lungs and liver.

BEAR'S GALL. The gall-bladder of a bear was valued as an alterative, anthelmintic, and nerve stimulant, and was used especially in hepatic and other abdominal diseases.

BEAR'S PAW. The skin of the foot, with the nails, of a species of bear. The bear's paw was considered a great delicacy, and was supposed to strengthen the constitution.

BIRD'S NEST. The gelatinous nests of several species of the swallow, *Collalia esculenta* and others, was regarded as a valued and expensive article of food, and was accounted a tonic and invigorating remedy for the sick.

CATERPILLAR. The dried larvæ was used in bronchial complaints and as a purgative and antispasmodic.

CENTIPEDE. The head and feet being rejected, the rest of the dried animal was reduced to powder. It was given for demoniacal possession, malarial fevers, obstruction of the bowels, for worms, and for snake bites.

CICADA SKINS. The exuviæ of a species of *Cicada*, or locust, was used for difficulties in speech; for dimness of vision and cataract; for bringing out the eruption of smallpox, and for convulsions and other diseases of children.

COCKLE SHELLS. The powdered shells of a bivalve mollusk were given for chills, and for intestinal obstruction.

CLAM SHELLS. The powdered shells were used for colds, chills, and fevers, and as a cathartic.

CORAL. In fine powder it was used to arrest hemorrhage from the nose and to remove nasal polypi. It was also applied to opacities of the cornea.

COW BEZOAR. A concretion (biliary calculus) found in the gall bladder of the cow was a remedy for chorea, smallpox, insanity, apoplexy, and palsy. It was given to newborn infants as a charm and prophylactic.

CUTTLEFISH BONE. The internal shell of a species of *Sepia*. Said to be styptic, alterative, and anthelmintic. In powder it was used locally to arrest hemorrhage, and internally for cancer.

DEER'S HORN. Hartshorn was formerly an expensive medicine, and all sorts of therapeutic properties were attributed to it.

DRAGON'S BONES. Fossil bones of the *Stegadon orientalis*, reduced to a fine powder. Used in ague, fevers, hemorrhages, and fluxes.

Dragon's Teeth. The fossil teeth of various animals were known by the name of dragon's teeth. They were supposed to act on the liver, and to be of service as cordial and sedative remedies.

Dried Frogs. The common frog dried without removing the skin or viscera. Soups and gelatin prepared from these animals were thought to be especially strengthening for convalescents.

Dried Mussels. The common salt water mussel dried. Claimed to be aphrodisiac; also a remedy for postpartum hemorrhage, for colic and intestinal obstruction.

Dried Toads. Skinned, eviscerated, and dried. They were said to be tonic and sudorific.

Dung Beetle. Gathered on the fifth day of the fifth moon, the feet and elytra discarded, and the insect roasted or boiled. Used for chills and fever, convulsions, and insanity.

Earthworms. They were reduced to powder and used as an anthelmintic; for fever, jaundice, ulcerated throat, snake and insect bites.

Elephant's Hide. A small piece of the skin of an elephant entered into the composition of certain plasters used for the cure of contusions.

Fossil Crab. In powder it was applied to ulcers, wounds, and snake bites; mixed with wine or oil it was given for chronic dysentery and pernicious fevers.

Fossil Shells. Undetermined species of fossil shells belonging to the genera *Spirifer* and *Rynchonella.* Held in the hands of parturient women they were said to facilitate delivery. Powdered they were applied to opacities of the cornea and to the eruptions of scabies; internally they were given for diarrhœa and hemorrhoids.

Fowl's Gizzard. The lining membrane from the gizzard of the common domestic fowl was prescribed in dyspepsia, diarrhœa, and urinary disorders.

Goat's Blood. The dried blood of the mountain goat. It was used as an application to bruises, and as a remedy for amenorrhœa and certain conditions following childbirth.

Haliotus Shells. The shells of *Haliotus funebris,* a bivalve mollusk. The outer layers were removed and the pearly portion reduced to fine powder, which is applied to opacities of the cornea and to the films of pterygium. It was also a remedy for diseases of the liver.

HEDGEHOG SKIN. The skin of the head of the hedgehog. A decoction of the skin was used for pulmonary complaints; powdered and made into pills, it was taken for the cure of skin diseases.

HUMAN FECES. Mixed with a large proportion of vegetable fiber, this was used as a remedy for hydrophobia, and as an antidote for certain poisons.

HUMAN HAIR. Human hair was reduced to charcoal by burning in a closed vessel and was given as a remedy for hematemesis.

HUMAN PLACENTA. The dried human placenta was considered a tonic in consumption. Roasted, it was given, in the form of pills, to parturient women to facilitate the expulsion of the fetus.

HUMAN URINE. The urine of children, to which common salt or calcium sulphate had been added, evaporated to dryness. It was given in debility, and in renal, vesical, and uterine complaints. It was also used as a lotion for sore eyes.

INNER MEMBRANE OF EGGSHELL. The dried membrane lining the inner surface of fowl's eggs.

IVORY. Supposed to be taken from a living elephant. The powder was believed to be stomachic, vulnery, and diuretic, and the jelly was a specific for rickets.

LARVÆ OF FLIES. The dried maggots of bluebottle and house flies. They were given as a remedy to cachetic and scrofulous children.

MAGGOTS. The dried larvæ of a species of *Eristalis*. Prescribed in the delirium of fevers, and for dysentery.

MOLE CRICKET. The anterior portion of the insect was used for polyuria and diarrhœa; the posterior portion for retention of urine and constipation. It was also used for difficult labor, hiccough, and bad ulcers.

MONKEY'S SKULL. Animals, or parts of animals, were enclosed in coarse clay vessels and subjected to heat until thoroughly carbonized. Thus prepared they were kept in shops and sold for medicinal purposes.

MUSK. The sac, containing musk, taken from the abdomen of the musk deer, *Moschus moschiferus,* was believed to purify the air, cure melancholy, and protect from the bites of serpents.

OX GALL. The dried gall bladder of the ox, with its biliary contents, was said to be tonic, stomachic, and laxative, and was used in the treatment of diseases of the digestive organs.

OYSTER SHELLS. The partially calcined shells of the oyster. They were said to be tranquilizing by nature, and in powder were used in malarial fever and various diseases accompanied by hypersecretion.

PANGOLIN SCALES. The scales from the body of *Manis javanica,* scaly anteater. Formerly used in all sorts of diseases, especially of the skin.

RHINOCEROS HORN. Tonic, alterative, and other properties were attributed to these horns. The decoction was taken in fever, smallpox, hemoptysis.

SCORPIONS. Roasted and powdered, this medicine was used for all forms of paralysis, for smallpox, scrofula, convulsions, and abdominal tumors.

SEA HORSES. Used as a stimulant; also had the reputation of facilitating parturition; it was sufficient that the patient hold one in her hand.

SEED PEARLS. Powdered and given internally for diseases of the heart and liver; externally applied to ulcers and opacities of the cornea, to the auditory meatus for deafness, and to the pustules of smallpox.

SILKWORMS. Washed in rice water, boiled in a decoction of ginger, and dried, they were used for convulsions in children, for menorrhagia, and as an aphrodisiac.

SILK COCOONS. They were burned, the ashes mixed with wine and taken internally in order to cause the bursting of abscesses.

SILKWORM MOTHS. Roasted moths. This medicine was thought to be aphrodisiac and a remedy for impotence.

SNAILS. The common garden snail collected in the fifth month. They were used for lameness, rectal prolapse, convulsions, retention of urine, etc.

SNAKE. Believed to be a useful remedy for abdominal pains. From its habit of hiding in hedges and crevices it was supposed that, mixed with other drugs, it aids them in penetrating the most secret recesses of the body.

SPARROW DUNG. The excrement of the common house-sparrow, mixed with powdered peppercorns and made into a mass with alcohol, was applied to the skin to produce local anesthesia preliminary to the opening of abscesses or extraction of foreign bodies from wounds.

SPIDERS. Used for fever sores, boils, and to neutralize the poison of snakes and venomous insects.

Tortoise Shell. Jelly made from the plastron, or the powdered shell made into pills or mixed up in cakes, was reported to be tonic, cordial, astringent, and useful in diseases of the kidneys. The ashes were given to parturient women and dusted upon wounds and ulcers.

The method of reasoning of the Middle Ages—pure deductive reasoning from accepted premises—formed the basis of the old systems of medication. From some general hypothesis, accepted without proof and believed to represent a truth of universal application, deductions were made about all diseases and all remedies. For example—to cite only the selection of medicines by the doctrine of signatures—it was believed that the Creator in providing plants and other objects for the service of man had stamped on them, at least in many instances, an unmistakable sign of their special remedial value. Many of the animal remedies listed were probably chosen by some imaginary relation between the characteristics of the medicinal material and the symptoms of the disease. Thus, cicada skins might have been selected as a remedy for difficulties in speech because this insect had the power of producing such a shrill and prolonged sound, and parts of snakes were used for the reason that it was thought this reptile could "penetrate the most secret recesses of the body" as it did crevices and hedges, and thus carry the remedy mixed with it to the seat of the trouble.

Francis Bacon upset the deductive sort of reasoning completely as a method of arriving at the truth in the material world, and today observation of facts, explanation of relations between facts, establishment of rational general principles, and scientific interpretation form the basis of our reasoning in applying and extending knowledge in the sciences. Under Bacon's system animal remedies were put to the test, and health-restoring and lifesaving specifics came into use.

The animal kingdom's contributions to materia medica now became important. Jenner's vaccination of James Phipps on May 14, 1796, with cowpox virus from the arm of Sarah Nelmes furnished an animal remedy with the power to prevent smallpox, one of the world's greatest scourges, which, it is estimated, in every twenty-five years deprived at least 15,000,000 human beings of life, and left millions disfigured, weakened, crippled, and sightless. We have learned that only one agent can keep smallpox in check, and that is

vaccination. We know, too, that this animal remedy has done its work so well that a dreadful scourge is almost forgotten.

Charles Edouard Brown-Sequard, at the age of seventy-two at a meeting of the Paris Societe de Biologie in 1889, described the now famous experiments he had performed upon himself by the subcutaneous injection of testicular extracts, which resulted in increased physical strength, improved appetite, regulation of bowel function, and increase of mental activity. His report stimulated research in internal secretions, and resulted in the development of organotherapy, and its firm establishment in the treatment of disease. Thyroid, pituitary, and epinephrine are now included in our pharmacopœia, while ovary, corpus luteum, mammary, and numerous other organotherapeutic products are used all over the world in fields in which they are practically alone.

Emil von Behring, working in Koch's Institute with Shibamiro Kitasato, demonstrated that the serum of animals immunized against attenuated diphtheria toxins could be used as a preventive or therapeutic inoculation against diphtheria in other animals, through a specific neutralization of the disease. After trying out the remedy in man, Behring began to produce it on a large scale in 1894, and it soon became recognized as the specific treatment for diphtheria.

No more striking example of North American research along this line can be given than the evolution of insulin by Banting and Best in 1922. This glycolytic extract with its power of increasing the metabolism of sugar is daily prolonging the activity and usefulness of persons afflicted with *diabetes mellitis.*

And now animal remedies have come into their own to such an extent that we cannot think of the most modern and successful of our medicinal agents without thinking of serums, vaccines, and organotherapeutic products in general. In fact, there is perhaps no better way of demonstrating the upward progress of medicine and pharmacy than by comparing the makeshift animal remedies of the past with the scientifically proven ones of the present.

MEDICAL AND PHARMACEUTICAL NOTES

PRESCRIPTION DEPARTMENT ACTIVITIES ANALYZED.—Valuable information that has never before been given will be found in "The Professional Pharmacy," by Frank A. Delgado and Arthur A. Kimball, a detailed cost and operations analysis of prescription-department activities of professional pharmacies, made as a major phase of the National Drug Store Survey.

It is not practical in an announcement this length to outline the contents of the professional pharmacy. However, it might be stated that over 75 per cent. of the sales volume of the professional stores studied was actual prescriptions. Sales volume of sample stores averaged $107,000 each. Thirty-five professional pharmacies occupied an average of 1,632 square feet. Answers to the following questions are furnished: To what extent, if any, have the specialty type of prescriptions grown over a period of twenty years? Have prescriptions in liquid, capsule and tablet form decreased or increased during the past twenty years? What is the financial outlay necessary to open a new store? What equipment is necessary? What population is necessary to support a professional pharmacy? What is the turnover, gross margin, operating expenses, and net profits of professional pharmacies?

Approximately 1,808 pharmacists open new drug stores each year in the United States, and were that part dealing with prescription ingredients brought to the attention of these pharmacists, it is believed that a saving of from $100 to $500 per store could be accomplished.

Two reports by the Bureau of Foreign and Domestic Commerce covering the professional activities of retail pharmacies have come from the National Drug Store Survey. The first dealt with the professional activities of thirteen commercial-type drug stores in St. Louis. It was entitled "Prescription Department Sales Analysis in Selected Drug Stores" and was issued, in 1932, by the U. S. Department of Commerce. Copies can be obtained from the Superintendent of Documents, Washington, D. C., at five cents each. The second report, recently completed, is entitled "The Professional Pharmacy—An Analysis of Prescription Department Activities," and presents a pic-

ture of the pharmacy which specializes in prescriptions and other items related to public health. This report, covering about eighty pages, is being printed in the *Journal of the American Pharmaceutical Association,* in four installments, July, August, September, and October, 1933, and will then be available in a paper-bound book at fifty cents each, less 10 per cent. in lots of six copies or more. Advance orders are requested, in order to judge the number of copies to be printed, and should be sent promptly.

The value of the information contained in this report is not believed to be confined to the proprietors of professional pharmacies. It contains much information which should be of practical value to the proprietors of commercial-type drug stores, in increasing their volume of prescription business and the profit possibilities of their prescription departments. Professors and students in colleges of pharmacy may find herein answers to some of the questions about which there has been conjecture. Drug wholesalers and manufacturers of chemicals, galenicals, and pharmaceutical specialties should find the list of leading ingredients, which was compiled after an analysis of 20,000 prescriptions, of particular interest. Pharmacists who are contemplating the operation of a professional pharmacy will find certain information particularly diercted to them. It is hoped, therefore, that all branches of the drug profession and trade will be in some way aided by the information presented in this report.

Castor Oil Soap.—Castor oil soap is readily prepared at dispensing counter, as follows: Solution of potassium hydroxide, 80 per cent. w/v, 2 fl. oz.; industrial alcohol, 1 fl. oz.; castor oil, 3½ oz. by weight; mix in a conical beaker and set aside in a warm place; in about ten minutes a yellow transparent jelly of castor oil soap is produced. *Liquor Cresol Saponatus.* The official formula contains a great excess of soap, and a good preparation can be made by shaking 5 fl. oz. of cresol with the above quantity of soap and adding sufficient water to produce 10 fl. oz. *Liquid Castor Oil Soap.* A syrupy liquid, which contains about 66 per cent. of soap, and remains liquid on keeping, can be made by mixing the above quantity of castor oil soap with sufficient water to produce 7½ fl. oz. *Ether Soap.* Liquid castor oil soap, 4 fl. oz.; Industrial alcohol, 1 fl. oz.; ether, 5 fl. oz. *Liniment of Turpentine, Modified.* Liquid castor oil soap, 2½ fl. oz.; camphor, ½ oz. oil of turpentine, 13 fl. oz.; water to make 20 fl. oz.

Mix the liquid soap with an equal volume of water, add 1 fl. oz. of the turpentine, and shake to emulsify. Dissolve the camphor in the rest of the turpentine, and add this, 1 or 2 fl. oz. at a time, to the primary emulsion, shaking well after each addition. Add sufficient water to produce 20 fl. oz. *Castor Oil Fatty Acids.* The fatty acids obtained from the liquid soap by means of dilute sulphuric acid form an amber-brown liquid with but little odor, and may be used as a substitute for oleic acid.—W. A. Knight. (*Pharm. J.*, 1932, 128, 222.)

CORN SILK?—Zein, heretofore little known outside of the laboratory or the museum exhibit of interesting curiosities derived from corn, seems now ready to join the growing list of industry's low-priced raw materials, with possible applications in fields including plastics, filaments, films, finishes, sizing, and adhesives. A vegetable protein, it is extracted from corn-gluten, a by-product in the manufacture of corn starch, and forms a hard, colorless amorphous solid of horn-like character. Zein, when crude, contains corn oil and other impurities, but properly manufactured it is tasteless and odorless.

The properties of zein have been the subject of frequent investigation since it was first described in 1821, and its composition is probably better known than that of any other protein. Perhaps most important of its characteristics is its resemblance in certain respects to cellulose and cellulose derivatives. Like them, it softens slightly but does not dissolve in water. It is insoluble in absolute alcohol, though it is readily soluble in less-concentrated alcohol solutions, such as 80 per cent. (by volume), and in many other solvents.

Likely applications of zein exist in many fields in which plastics and resins are used. Solutions of zein when evaporated to dryness leave a transparent continuous film capable of being dyed and filled, and of being plasticized, like cellulose derivatives, to overcome the natural brittleness of the film. Or, as zein is miscible with numerous cellulose derivatives, it may be used as a filler in sheets or molding compounds, apparently causing no impairment in strength when so used.

Filaments of zein have been made in the laboratory. These, unlike the common artificial silks, are of protein matter, and therefore more nearly approximate natural silk in chemical composition. At present, improvement must be made in the physical properties of zein

fibers before they can be considered seriously for the manufacture of artificial silk. The possibilities are interesting to contemplate, however.

The resistance of zein to water, its non-putrescence, non-inflammability, indicate its advantageous use for certain purposes as an adhesive, in sizing and coating paper and textiles, and in finishing leather or leather substitutes. On the other hand, since it dissolves in dilute caustic solution with the formation of sodium zeinate, zein may be used for a water-soluble, as well as for a spirit-soluble base. Its main applications will probably lie in the fields indicated, but recent experiments with zein as a reënforcing compounding material for rubber, as an example, indicate that, like all products ready for introduction on an industrial scale, it is likely to develop numerous applications at present unforseen.—(*A. D. Little Bulletin.*)

Sodium the Metal—The familiar and vitally essential compound, common salt, contains just under 40 per cent. by weight of the element sodium, which is also present in glass and water-glass, in soap, and in practically all washing preparations, but the metal itself is a stranger to most people. Sodium is, however, one of the commonest elements in the crust of the earth. It is about as plentiful as potassium and magnesium, and is exceeded in plentifulness only by the metals calcium, iron and aluminum, and the non-metals oxygen and silicon. There is perhaps ten times as much sodium in existence as there is of all the heavy metals, except iron, put together. Besides the immense amounts locked up in the rocks of the earth, there occur the more available rock salt, the 3 per cent. solution of salt in the ocean, and smaller, yet important, local sources of such compounds as the carbonate (trona), the nitrate and the sulfate.

Metallic sodium, known scientifically since 1807, is made on a large scale by the electrolysis of caustic soda. The commercial metal, of better than 99.9 per cent. purity, sells for about 20 cents per pound in drum lots, as 12-lb., or smaller, cast bricks. It is very light (0.97 compared with 2.7 for aluminum and 8.94 for copper), melts at 208° F., and boils at a bright red heat (1616° F.). An alloy of 68 per cent. potassium and 32 per cent. sodium is liquid down to about 15° F., although it is somewhat pasty below 45° F.—(*A. D. Little Bulletin.*)

BOOK REVIEW

THE MODE OF ACTION OF DRUGS ON CELLS. By A. J. Clark, B.A., M.D., F.R.C.P., F.R.S., Professor of Materia Medica in the University of Edinburgh. 298 pages. The Williams and Wilkins Company, Baltimore, Md.

Two or three years ago at the annual meeting of the Federation of Biological Societies, a group, consisting of nearly all the well-known pharmacologists of this country, sat together one evening discussing informally the function and purpose of pharmacology. There were obviously two distinct opinions on this subject. One group, interested in the utilitarian viewpoint, considered the science of pharmacology as a branch of medicine. The other group, with an academic interest, would place pharmacology among the biological sciences.

Emphatically, Professor Clark belongs to the latter group. While he does not entirely lose sight of the fact that the *raison d'être* of pharmacology is that it may ultimately contribute to the art of therapeutics, his personal interest, as revealed not only in the present volume but also in his earlier work, "Applied Pharmacology," is evidently in the academic aspect of the science.

This is not the place to defend the abstract scientists; men who delve into the secrets of nature with no other motive than curiosity to know how she works, to determine the fundamental laws which govern natural phenomena. These men are not merely amusing themselves in philosophical speculations, but out of their discoveries arise not infrequently practical applications of the utmost value to industry and the arts. Had Sir William Crookes not been interested in the ultimate structure of matter Roentgen would not have been able to make practical application of the X-ray.

The problem of the mode of drug action is so patently of enormous practical importance in the synthesis of new remedial agencies that no one dare sneer at such scholastic pharmacology as represented in this volume.

Unfortunately, we are so ignorant concerning the laws of colloidal chemistry, and the basic structure of cells, that none of our theories of drug action can be regarded as scarcely more than speculations. As Professor Clark says, "There is indeed very little direct evidence that the biological response is produced by a chemical reac-

tion between the drug and the cell constituents. This assumption is chiefly justified by the facts that it is supported by much indirect evidence, and that there is no alternative hypothesis which has stronger evidence in its support." And yet the fundamental concept of his whole philosophy is based on the theory that drug action is the result of chemical union between cell-molecule and drug-ion. It may seem foolish to attempt to postulate laws when we are so profoundly ignorant of the fundamental facts, but let us remember that our ignorance of what is the force of gravity does not prevent us from discovering the laws of its operation.

While much of this book is—and by the very necessity of this subject must be—distinctly classified as "highbrow," in the enormous collection of facts from all sorts of sources there is a wealth of material to interest any one with the slightest degree of scientific curiosity in his mental make-up. For example: the author in discussing the comparative size of the cell and the molecule of acetyl-choline says, "This is about the relation between a large whale and a small midge. The problem is to form some picture of cell structure that will explain the fact that a few thousand of these molecules, when they unite with the cell, suffice to modify its function."

Does it not cause one to stop and think when we are told that the human eye is capable of detecting fluorescine in a "concentration of one part in 10^{15}" (write fifteen ciphers after the 10); or that the number of cells in the human body of an ordinary man is roughly 260,000,000,000,000 and that Cameron in 1926 calculated the number of molecules in a single blood-cell to be in the thousands of millions.

It is a well-known fact that many drugs exert primarily a stimulant effect followed with functional depression. Following the lead of Straub, Professor Clark has marshalled a mass of evidence to indicate that the first effect of the drug is due to its surface action, that is, upon the outside of the cell, and that the secondary effects occur after the drug has penetrated into the cell protoplasm.

After one has read the chapter on "Individual Variation in Population," he perceives why, in the very nature of things, it is impossible that a biological assay can ever be accurate in the sense of a chemical assay. For example: Tattersfield and Gimingham have found that, out of 100 aphids, two will be killed by a concentration of nicotine of 0.01 mols per 100 litres and that two will survive a concentration of 1.2. The medium lethal dose does not lie at the mathematical mean of these two figures, for one-half of the aphids is killed by a concentra-

tion of 0.25. The standard deviation in the case of digitalis on cats' hearts, however, is only 12.15 per cent. and hence biologic standardization of this drug is reasonably satisfactory.

To those who have any trace of scientific philosophy in their mentality, or who are interested in present-day trend in pharmacological science, we can cheerfully recommend this book as practically unique, and while it reaches into the tenuous intellectual atmosphere, it is both readable and thought-provoking.

H. C. Wood, Jr.

Argyria or Silver Sickness—A brand-new method for detecting a strange disease, argyria, in its earliest stages was reported to the American Medical Association by Dr. Irving S. Wright, of New York Post-Graduate Medical School of Columbia University.

Argyria is a condition in which the patient turns a greyish-blue color. In the final stages the color is very pronounced, and if the patient is exposed to sunlight, his skin turns a very dark mahogany brown. The condition is becoming more common all the time. There is no way of treating it.

Argyria results from taking medicines containing silver salts for a long period of time. Such medicines are often given in the treatment of nose and throat ailments.

Formerly it was thought that the blue discoloration, which makes its first appearance around the base of the nails, was due to stoppage of the blood flow through the tiny blood vessels, the capillaries. Using a specially developed microscope, Dr. Wright and his associates examined the capillaries of the nail cuticle in cases of argyria. They found that there was no stoppage of the blood flow and no evidence of congestion. This led to discovery that continued administration of silver-containing medicines results in the precipitation of silver albuminate in the tissues, which produces the blue color.

Once the color is established, there is no satisfactory remedy for the condition. But if the first appearance of it around the nails is noted and the dosage of silver-containing medicines stopped, it is believed the condition will not go farther. While the condition does not impair the health, it is most disfiguring.—(*Science News Letter*, August 5, 1933.)